

REGIONAL ILEITIS

REGIONAL ILEITIS

SECOND REVISED EDITION

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Preface to the Second Edition

TWENTY FIVE YEARS have passed since the original paper on Regional Ileitis was read by Crohn, Ginzburg, and Oppenheimer at the meeting of the American Medical Association at New Orleans in June 1932. Acceptance of the clinical concept throughout the scientific world was prompt and a voluminous literature has since been amassed. What was first considered to be probably a rare and unusual disease is now regarded as a malady of wide pread distribution affecting all ages and climes and socio-economic strata of the world population. What began as a pathologic entity involving only the terminal ileum rapidly evolved to a regional or more diffuse enteritis and was soon expanded to include a generalized ileo jejunitis. In more recent years the inclusion of the duodenum and the stomach has been recognized—in one published case even the esophagus was cited. Combined forms of ileitis and colitis were seen and described as early as 1935, resulting in a confused clinical picture that threatened the concept of ileitis and colitis as being independent and unrelated pathologic and clinical entities.

From this small beginning we have witnessed the evolution of a Frankenstein monster that if not threatening to life frequently results in serious illness, often prolonged and debilitating. Surgery can control this problem fortunately and usually with success.

The first edition of this monograph, published in 1949, encompassed approximately 300 cases. At the writing, our experience is based on over 676 cases of diverse types of enteritis with a fairly successful follow-up of our personally recorded cases. The present study consists of 542 cases of regional or terminal ileitis, 70 instances of diffuse ileo jejunitis and 64 examples of so-called combined ileo-colitis. Thus the writing of the life history of the disease has become a possibility and a proximate evaluation of the medical and surgical treatment which is constantly in a state of flux can at least be essayed as of this date.

This new edition is warranted, we feel, if only for the attempt to bring up to date the follow-up of medically treated cases and to ascertain the true figure of recurrences after operation. So much has been said of late in the press concerning the effects of treatment (particularly surgical)

in ileitis so many loose statements have been made that a true unprejudiced appraisal is already overdue

The cooperation of my associate Dr Harry Yarnis in collating the clinical data and most important in the follow up of the case has been of invaluable assistance The inclusion of the chapter on Roentgenography by so capable and experienced a radiographer as Dr Richard H Marshak will greatly enhance the value of this book as will the chapter by Dr David A Turner on Intestinal Absorption in Regional Ileitis a subject which truly belongs in the province of the bio chemist

I am much indebted to my confreres at Mount Sinai Hospital for unstinted cooperation and to the medical and surgical profession at large who have made our office a consultative repository of vast amounts of clinical material

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BURRILL B CROHN M D

Contents

PREFACE TO THE SECOND EDITION	v
LIST OF TABLES	x
CHAPTER	
1 GENERAL CONSIDERATIONS SCOPE OF STUDY	1
Historical Background	2
Regional Ileitis	4
Scope of the Present Study	6
2 REGIONAL ILEITIS ETIOLOGY (542 Cases)	8
Etiology	8
Specific Agencies	9
Protozoa	11
Bacillary Dysentery	11
Viruses	12
Sarcoidosis	13
Trauma	14
Familial Incidence of Ileitis as a Possible Etiologic Factor	18
Theories Regarding the Pathologic Mechanism in the Creation of Ileitis	21
Vascular Changes	22
The Theory of Lymphatic Block	23
Age and Sex in Regional Ileitis	26
Psychomatic Factors	28
Social Status Race Nationality Religion	30
3 GROSS PATHOLOGY	32
Microscopic Pathology	37
4 CLINICAL FEATURES	42
Onset	42
Physical Examination	48
Obstructive Phenomena	51
Pancreatic Insufficiency	51
5 FISTULA FORMATION IN REGIONAL ILEITIS	52
Internal Fistulas	54
Perirectal Fistulas	57
Method of Anal Fistulation	58
6 THE COURSE IN REGIONAL ILEITIS	61
Group 1 Chronic Long standing Regional Ileitis with Spontaneous Healing	62
Group 2 Chronic Regional Ileitis without Progression	62
Group 3 Chronic Regional Ileitis with Progressive Extension (Mucosal Type)	66

7	COMPLICATIONS OF REGIONAL ILEITIS	71
	Perforation of Intestine 71 Hemorrhages 71	
	General Complications 72 Gynecologic Manifestations 74 Pregnancy as a Complicatory Factor in Ileitis 74	
8	RADIOGRAPHIC DIAGNOSIS OF REGIONAL ILEITIS ILEO JEJUNITIS AND ILEOCOLITIS by Richard H. Marshall	77
	Nonstenotic Phase 77 Stenotic Phase 83	
	Ileum 85 Ileo jejunitis 88 Jejunum 89	
	Duodenum 92 Recurrent Ileitis 92 Healing in Regional Enteritis 92 Regional Enteritis with Involvement of the Colon 93 Combined Disease 94	
9	THE DIAGNOSIS OF REGIONAL ILEITIS	108
	Differential Diagnosis 112	
10	PROGNOSIS IN REGIONAL ILEITIS UNDER MEDICAL OR CONSERVATIVE TREATMENT	117
11	MEDICAL THERAPY CONSERVATIVE PALLIATIVE TREATMENT OF REGIONAL ILEITIS	121
	General Directions 121 Diet 121 Ambulation 124 Various Medications 125	
12	INDICATIONS FOR SURGICAL INTERVENTION IN REGIONAL ILEITIS	128
	Indications for Operative Interference 128 Contraindications for Surgical Intervention 129 The Timing of the Surgical Attack 129 Type of Operative Procedure 130	
13	SURGICAL TREATMENT OF CHRONIC REGIONAL ILEITIS HISTORICAL SURVEY	132
14	A REVIEW OF OUR OWN EXPERIENCE WITH OPERATIVE PROCEDURES FOR REGIONAL ILEITIS	138
	Type of Operative Procedure 138 Recurrence 140 Diagnosis and Treatment of Recurrences 144 Treatment of Recurrent Ileitis 145	

15	ACUTE REGIONAL ILEITIS	148
	Historical Survey 148 Site of Disease 149	
	Appearance of Lesion at Operation 149 Clinical	
	Manifestations 150 Radiographic Picture 150	
	Differential Diagnosis 151 Follow up of Acute	
	Ileitis 152 Distinct Entity or Part of Chronic	
	Regional Ileitis? 153 Eventual Outcome of Cases	
	of Acute Ileitis 154 Medical or Surgical Treat-	
	ment of Acute Ileitis 155	
16	ILEO-JEJUNITIS	157
	Various forms 158 Etiology 165 Pathology	
	166 Symptomatology 168 Differential Diag-	
	nosis 174 Whipple's Disease 179 Primary	
	Jejunal Ulcer 180 Granulomatous Disease of the	
	Duodenum and Stomach 180 Clinical Symptoms	
	181 Radiologic Features 182 Diagnosis 182	
	Treatment 182	
17	MALABSORPTION IN ILEITIS <i>by</i> David A. Turner	183
18	PROGNOSIS AND TREATMENT OF ILEO JEJUNITIS	200
	Follow up of Medically Treated Cases 200	
	Follow up of Surgically Treated Cases 200 Med-	
	ical Therapy 201 Surgical Intervention 203	
19	ILEOCOLITIS <i>by</i> Harry Yarnis	207
	Historical Review 207 Etiology 211 Clinical	
	Features 212 Medical Therapy 215 Surgical	
	Management 216 Prognosis and Results 219	
	REFERENCES	220
	INDEX	236

List of Tables

TABLE	PAGE
1 Age Distribution at Onset	26
2 Age Incidence in Regional Ileitis (Ravdin & Johnston)	26
3 Age at Onset	27
4 Age Incidence in Childhood (Schiff)	28
5 Anatomic Distribution in Regional Ileitis	32
6 Duration of Symptoms before Recognition of Regional Ileitis	42
7 Variations of Internal Fistulas	55
8 Type of Fistulas in Regional Ileitis	57
9 Medical Follow up (85 cases)	118
10 Mortality under Medical Observation	119
11 Surgical Treatment of Chronic Regional Ileitis	135
12 Type of Operations for Ileitis and End Results	138
13 Primary Group Follow up	139
14 Follow up of Surgical Cases	140
15 Follow up of Acute Ileitis (Old Series 1949)	152
16 Follow up of Acute Ileitis (Recent Series 1957)	153
17 Ileo Jejunitis Age Incidence	166
18 Ileo Jejunitis Follow up of Medically Treated Cases	200
19 Ileo Jejunitis Follow up of Surgically Treated Case	200

REGIONAL ILEITIS

Chapter 1 / General Considerations, Scope of Study

THE TERM REGIONAL ILEITIS was created in 1932 to describe what was considered a new pathologic and clinical entity—a clear cut disease affecting the terminal segment or segments of the small bowel characterized by a subacute or chronic necrotizing and cicatrizing inflammation. While the term regional ileitis is still the most popular denomination of the disease many other descriptive names have been created by successive authors to cover new and expanding concepts of the anatomic and pathologic aspects of this malady. Terminal ileitis was the first designation because in the original publication the first 14 cases were all restricted anatomically to the terminal 8 to 12 inches of the ileum. Regional ileitis however denoted a more widespread distribution. Regional enteritis was suggested by Brown, Barger and Weber; chronic cicatrizing enteritis by Harris, Bell and Brunn and by Cushway; chronic ulcerative enteritis by Corr and Boeck; segmental enteritis by Lewisohn to denote both the tendency to scar formation and the more widespread anatomic distribution while ileocolitis was suggested by Erb and Farmer and again by Colp to indicate the not infrequent involvement of the colon. To this concept was soon added ileojejunitis—the same pathologic process extended to include anatomically all of the jejunum continuously or segmentally. In more recent years the literature has encompassed cases of the same granulomatous process involving the duodenum, the stomach (rarely) and in one case the esophagus. These rare instances are regarded as pathologically identical to that described for the small bowel and require no new terminology. Finally ileocolitis was created to cover those combined cases where some segments of the large as well as the small bowel are concerned.

As originally described regional ileitis or enteritis was a nonspecific inflammatory disease—one of the larger group of intestinal granulomata—a process affecting mainly young adults and characterized by an acute, a subacute and a chronic phase of necrotizing, ulcerating and cicatrizing inflammation. The disease is further marked by its tendency to fistula

to the extent of about 18 inches was distended thickened in the coat externally of a reddish color and internally covered by numerous well defined ulcers varying in size from a diameter of a split pea to that of a sixpence. After a lapse of almost a century the English literature again contained a case report by Moynihan in 1907 entitled *The Mimicry of Malignant Disease in the Large Intestine*.

In the meantime the German literature rapidly began to show an abundance of references to non specific granulomata of inflammatory nature. Braun in 1901 quoted 5 cases mostly of traumatic or hernial origin and later cited 25 more cases from the current periodical up to 1909. By 1920 Tietze had collated 281 references on this subject including at least 2 cases of typical regional or terminal ileitis (Lowen and also Willman). The literature now increased apace. Dalziel contributed an excellent article and the whole subject crystallized with a paper by Fischer and Lurmann (1933). This paper which included the description of 3 cases of typical regional or terminal ileitis recognized and granted priority to our original publication less than a year previous in this country.¹¹ The discussion before the German Congress and thereafter was amplified by the experience of such noteworthy surgeons as von Haberer Gisbertz Peters Anschutz and Fenster.

By 1925 American writers had become cognizant of the subject of nonspecific granulomata of the intestinal tract. Coffen in 1925 Horsley (including 2 fine case descriptions of ileitis) and an excellent study by Moschowitz and Wilensky (including an admirable photographic reproduction of ileitis) of 4 cases of granulomata of which one was typical of ileitis as we now know it. Mock in 1931 summarized the subject of infective granulomata attributing most of these pathologic masses to some interference with vascular supply to a given tissue resulting in local necrosis followed by a proliferative reparative tissue reaction. He considered trauma to be the most common etiological agent. His cases many of them due to penetrating foreign bodies diverticulitis strangulated hernia silk and metallic ligatures involved the sigmoid stomach omentum splenic flexure and in one case participation of the terminal ileum. Golob added one case and Erdmann and Burt 5 more 2 of which had typical involvement of the terminal ileum with intestinal obstruction and internal fistulas from ileum to cecum. Finally in 1933 Ginzburg and Oppenheimer reported a group of 52 instances of nonspecific granulomata of the intestinal tract these cases were the result of vascular disturb

formation within adjoining loops of the small and large bowel by external fistulas to the abdominal wall and by frequent rectal suppurative complications. A disproportionate increase of connective tissue may and frequently does lead to intestinal stenosis and obstruction. Clinically the disease is featured by fever, diarrhea, loss of weight, a secondary anemia, and the formation of an intra-abdominal mass constituted by approximated loops of inflamed intestine frequently joined together by internal fistulas. The process regularly begins or stops at the ileo-cecal valve, the exceptions to this localization being few in number. The disease may extend upward by skip lesions separated by healthy skipped areas. It is rarely a progressive lesion; it may remain for twenty or more years strictly localized in the terminal ileum. Progression of the disease and involvement of nearer or higher areas frequently result after attempts at surgical cure; the original focus of disease if not molested may increase in intensity and severity but will not extend in an anatomic progression. Recurrences of the inflammatory process after palliative or radical surgical procedures further characterizes the process as an active, persistent and recurrent disease.

HISTORICAL BACKGROUND

Nonspecific granulomata of the alimentary tract involving mainly the large bowel have been recognized for many years. The great pathologist Morgagni (1682-1771) in his *De Sedibus et Causis Morborum* reported cases of enteritis with particular involvement of the ileum as pointed out by Hymen I. Goldstein. The European medical literature has been replete with innumerable examples of such inflammatory masses located in large and small intestine, some even in the stomach. Included in these descriptions undoubtedly are many instances of what we recognize now as typical ileitis or enteritis. In 1813 Combe and Saunders reported before the Royal College of Physicians of London "A Singular Case of Stricture and Thickening of the Ileum." To quote in part: "The lower part of the ileum as far as the colon was contracted for the space of three feet to the size of a turkey quill." John Abercrombie discussed pathologic states of the ileum and reported cases very similar to regional ileitis. His description published in 1828 is instructive. A girl aged 13 about a year before her death (1814) began to be afflicted with pain of the abdomen and frequent vomiting. The caput coli 3 inches along the ascending colon and the lower end of the ileum

Three years after the first designation of regional enteritis as an entity Binney was able to collect 267 cases from the literature in 1939 Ravdin and Johnston catalogued 393 cases from current periodicals Confirmatory reports from the English literature were not long in making their appearance (Jackman Hadfield Barbour and Stokes Molesworth Hurst and his co authors) as likewise from the Dutch literature (Groen and Pompen Snijper Pompen and Groen)

A dissident viewpoint was advanced by several writers who considered regional ileitis a clinical but not a pathologic entity because of the occurrence of the disease at various other areas of the intestines Characteristic lesions involving the jejunum were shown in 2 cases (Harris Bell and Brunn) of 18 cases reported from the Mayo Clinic in 1934 (Brown Bergen and Weber) the ileum was involved in 9 the jejunum in 3 the terminal ileum and parts of the colon in 11 instances Homans and Has while recognizing typical terminal ileitis questioned the localization of the process and felt that the jejunum was more often involved than was then recognized They thought that the appendix was possibly an important etiologic factor they further remarked for the first time that the disease might have a predilection for Hebrews (Mixer) a theory that has since been disproved Meyer and Row emphasized the involvement of the mesentery particularly in fistula formation Erb and Farmer emphasized the acute phase in children as it simulated appendicitis Reichert and Mathes made the first suggestion regarding etiology namely experimental lymphoedema by blocking lymphatics Goldfarb and later Kantor gave the first veritable description of the roentgen appearance of the disease in the terminal ileum as the string sign

Actually considerable knowledge has been added to the original concept of terminal or regional ileitis in the last twenty five years The anatomic and pathologic states have been extended to include the upper reaches of the ileum and all of the jejunum even duodenum and stomach opportunity has been afforded for studying the life history of the disease its progression and extensions Acute ileitis if such a concept exists has been analyzed and its subsequent course has been traced Above all prognosis has been learned and finally medical and surgical approaches to therapy have been tried some discarded newer methods apprehended The whole problem of recurrences with their increasing frequency and severity has had to be acknowledged and a rational method of recognition and treatment of these recurrences has been attempted

ances herniation and sealed-off intestinal perforations and included several examples of the entity which had already been isolated and termed regional ileitis.

This large group of nonspecific inflammatory granulomata involved any or all parts of the alimentary tract and omentum. They formed masses often obstructive in nature that usually simulated in their clinical course the picture of a new growth. They were characterized by a piling up of granulation tissue with various stages of ulceration, necrosis and fibroblastic proliferative secondary reactions. The histologic process consisted of round cell infiltration, fibroblasts, connective tissue stroma and new blood vessel formation with the occasional occurrence of giant cells of unusual magnitude (Moschowitz and Wilensky). Etiologic agents apart from trauma and foreign bodies were not recognized. Tuberculosis, syphilis and actinomycosis were excluded by definition.

REGIONAL ILEITIS *

From this large and general group of nonspecific granulomata of the intestinal tract a subspecies termed regional ileitis was isolated, a distinction which was possible because this group was characterized by a consistent anatomic distribution, a characteristic clinical course, a progressive life history and typical complications of fistula formation and obstruction. Also this group was further amenable to successful surgical interference. It is interesting to note historically the amplification of the original concept of terminal ileitis. The first report covered 14 cases of a typically characteristic disease involving only the terminal segment or segments of the ileum. Acute cases were included among those running the more easily recognized chronic inflammatory course. Shortly thereafter (1933) the involvement in some cases of the upper reaches of the ileum and all or part of the jejunum as noted by Harris, Bell and Brunn led to the identification of ileojejunitis either as an extension or a continuation of terminal ileitis or as a subgroup per se in which the involvement of the terminal segments of the small intestine was subordinated to the process higher up. The participation of the colon segmentally either by contiguity from the terminal ileum or by scattered areas of coincidental disease was first noted by Colp (1934) and subsequently by Crohn and Rosenik (1936) and led to the creation of still another subgroup, ileocolitis (Crohn and Berk) denoting a most confused and complicated pattern of involvement of ileum and varying segments of the large bowel.

because of their own identifying characteristics though some confusion will arise when attempts are made to separate true primary acute ileitis from acute exacerbations of chronic recurrent ileitis. In fact some doubt has been raised as to whether such a syndrome as "acute ileitis" does actually exist or rather that such acute manifestations really represent sudden exacerbation of a smoldering, chronic pathologic state.

The group of ileojejunitis and duodenitis has been considered separately because the involvement of the whole or of most of the small bowel introduces new elements of clinical significance and misses many of the distinguishing characteristics of the terminal form. Its life history is different its therapeutic approach is entirely singular its differential diagnosis and prognosis call for a more novel viewpoint. The fourth category of combined ileitis and colitis is so confusing with so many cross elements and complications and is so difficult a problem in therapy particularly with regard to successful surgical treatment that it requires its own generic consideration.

The truly encyclopedic review and experience at the Mayo Clinic published in 1954 by Von Patten et al encompassing an extensive group of 600 cases, represents a massive addition to our present knowledge of the disease particularly valuable is the superb follow up of their cases over many years which is incomparably complete

SCOPE OF THE PRESENT STUDY

This study is an analysis of instances of segmental enteritis which have been under our own personal office and hospital care during all or part of the last twenty five years. These cases are all private patients who have been observed carefully treated and subjected to continuous analysis including follow up during this period. Some were included in the original group that constituted the first 14 cases published in 1932 as terminal ileitis. The remainder have been registered during all of the succeeding years the last addition to the list having terminated approximately six months ago (January 1957) to allow for some albeit inadequate follow up. Ward cases in hospitals are not included those that are listed were accepted only because they elicited treatment and were registered as personal patients even though the previous surgical or medical treatment had been administered elsewhere. For purposes of analysis and study this larger group may be subdivided into four essential categories (1) Regional Ileitis—the acute and chronic forms 342 cases (2) Ileocecalitis 64 cases (3) Involvement of duodenum and stomach 6 cases (4) Combined cases—ileitis with involvement of some of the large bowel 64 cases (Total 676 cases)

All four categories represent types of regional or cicatrizing enteritis. They are not distinct entities in first mixed forms are not unusual. The identical pathogenesis and pathologic histology is common to them all. But they differ sufficiently clinically and anatomically to merit consideration as separate groups. Each group has identifying characteristics its own life history and prognosis as well as its individual approach to therapy.

The largest group of cases of ileitis comprises the bulk of the study and provides the greatest number of the classic variety of the disease in which the ileum particularly the terminal segments of small bowel is involved. The disease being one of low grade pathogenicity and chronicity requires that this group be identified as chronic regional ileitis. In contradistinction the acute case have been separately considered

and chickens and proved negative in 5 of the original cases. Subsequently whenever a suspicion of tuberculosis has arisen the most careful procedures have been followed to eliminate the Koch factor as an etiologic agency. When tubercle bacilli have been demonstrated in cut sections or when guinea pig inoculations have been positive the case has been considered as intestinal tuberculosis simulating ileitis. Frazer and Hagar reported a case of regional ileitis resected in which the mesenteric lymph nodes showed old caseating tuberculosis; the specimen of ileitis itself was free of any evident invasion by the tuberculous process and was nonspecific granulomatous in nature by histologic study. A total of 762 cultures and 131 inoculated animal (including guinea pigs, rabbits, cats, chicken and rats with material from lesions of 43 patients) failed to give positive results for *Mycobacterium tuberculosis* (Van Patter).

Syphilis and actinomycosis, two specific infections that may involve the intestine, have been excluded as an etiologic agency because of the fact that serologically syphilis and histologically actinomycosis are easily differentiated and excepted.

Specific Agencies

Many authors have found various bacteria in cultures of tissues or in peritoneal exudates and have implied that these bacteria were the etiologic agents of the disease. This occurred many times in the earlier publications after the disease was first described; recent literature has made no such claims and no such confutations. Erb and Farmer, in one case, found in stained sections of the involved gut gram negative bacilli apparently of the *B. coli* group. By culture they obtained a similar organism from the ileal mucosa, mesenteric lymph glands, liver and bile. In their comment on the findings, Ravdin and Johnston point out that these tissue cultures were taken eight hours after death and that no specific agglutinations against the patient's blood had been essayed. Ross has found similar bacteria in one case, an anaerobic streptococcus from the peritoneal fluid, from the mesenteric lymph nodes and from the deep surface of the intestinal ulcerations. Peters found the usual enterococcus of intestinal type in the cultures of superficial tissue but no bacteria in the sections of deeper tissue. Jackman, in 2 cases of acute ileitis, was not able to demonstrate bacteria in the deeper layers of the resected specimens. Others have found gram positive cocci in the submucosa (Konjetzny), enterococci in stool cultures (Fischer and Lurmann), aerobacteria, aero

Chapter 2 Regional Ileitis Etiology (542 cases)

REGIONAL ILEITIS is a non specific chronic recurrent granulomatous disease, affecting mainly young adults and characterized by a necrotizing, ulcerating inflammatory process one in which cicatrizing elements in the long enduring crises is an important feature. The terminal ileum is apparently the parent seat and origin of the pathologic process though the whole ileum may be involved. Typically the process rests at the ileo cecal valve transcending that barrier only exceptionally. Clinically the disease is marked by a low grade fever abdominal pain most frequently by mild diarrhea and by progressive loss of weight and a secondary anemia. The occurrence of an intra abdominal mass is frequently noted. The most striking clinical feature is the formation of fistulas of ileal origin these fistulas leading from ileum to the abdominal wall or from ileum to other loops of bowel or other hollow viscera. Rectal complications of a suppurative nature constitute a striking manifestation of the disease. The pathologic process is an enduring one lasting over the course of many years. Eventually intestinal obstruction and hemorrhage may intervene open perforation of the small bowel is extremely rare. Spontaneous cure are minimal but may often occur surgical intervention is still the therapeutic method of choice.

ETIOLOGY

The true causation of ileitis remains unknown despite diligent efforts to a certain a bacterial or specific agent is the factor in its initiation. It was of first importance to exclude tuberculosis as the specific infecting agency. Much confusion in the past has evolved from the inclusion of case of non specific ileitis within the category of hypertrophic ileocecal tuberculosis. All resected specimens of ileitis have been conscientiously subjected to careful histologic study careful staining methods for the recognition of the Koch bacillus in cut section to cultures and animal inoculation.

Material from the bowel wall of the ileum and from the enteric nodes in the early resected case were inoculated into guinea pigs rabbits

Protozoa

The *Entamoeba histolytica* was implicated by Corr and Boeck on the basis of one case finding. However the typical pathologic lesion of amebiasis were absent from other segment of the large bowel as is characteristic of amoebic infestation. No other authors in the literature have made similar claims. In other instances *Trichocephalus dispar*, *Oxyuris vermicularis*, *Giardia lamblia* and other parasites have been found in the stool examinations but never sufficiently consistently as to imply that their presence was the cause of ileitis.

Foreign bodies which play so large a role in granulomata of the intestinal tract such as fish bones, metal ligatures, food residues, pits and fragment of bone are absent from cases of true regional ileitis or jejunitis. Large giant cells are regularly found in histologic sections of ileitis; these giant cells are not tuberculous or syphilitic in origin. They are best explained on the basis of foreign body inclusion; but the extraneous substances that give rise to such giant-cells are not gross or material in substance. They are probably in some instances due to (a) lycopodium spore from dustings of surgical gloves or a previous surgical intervention or to (b) minute fragments of food detritus collected and secondarily caught in the ulcerated pockets of the mucosa.

Bacillary Dysentery

Felsen claimed a common source of origin for a large percentage of the cases of distal ileitis, chronic ulcerative colitis and nonspecific granulomata. This concomitant agent was in his belief the *Shigella dysenteriae*. In a follow up of 400 cases of acute bacillary dysentery he found 29 cases of acute distal ileitis, 22 cases of chronic distal ileitis, 18 cases of combined chronic ileo-colitis and 84 cases of chronic ulcerative colitis. His study included a survey of the late end results of the epidemic of bacillary dysentery which occurred at Jersey City in September 1933. He gave 84 cases with high serum agglutination against *Shigella dysenteriae* and 8 with positive stool culture. He describes particularly an acute dysenteric appendicular form with involvement of the small bowel and various types of mixed forms involving terminal ileum and colon. His classification and acceptance of dysentery is based upon agglutination titers of 1:100 and over except for the Sonne Duval type in which he accepts 1:50 as significant. Positive stool cultures were obtained in 10 of 70 cases examined.

genes (Halligan and Halligan) Mailer found streptococcus viridans in 2 of his cases

These various observations are of interest but fail to give consistent findings which would regularly implicate a single causative bacterial agency. Numerous attempts by staining by aerobic and anaerobic cultural methods and by animal inoculations have similarly failed to uncover a singular offending agency.

A most serious attempt to investigate the bacterial etiology of the disease was made by Pumphrey at the Mayo Clinic. Thirteen cases of granuloma of the bowel were studied, 10 of which were typical regional ileitis. Cultures were taken by sterile technic in the operating room from resected specimens and regional nodes. The specimens were macerated and planted in media such as blood agar, eosin methylene blue plates, dextrose brain broth, chick mash overlaid with paraffin and agar slants. Many organisms, gram positive and gram negative, were recovered, none of which could be said to be predominant throughout the series. In no instance was he able to isolate an organism of the dysentery group. None of these bacterial cultures were consistently agglutinated by the serum of the patient from whom the culture had been obtained, nor by the serum of other patients suffering from the same disease. Cultures from the throats of 2 patients with the disease yielded streptococcus viridans. The injection of these cultures into rabbits failed to reproduce the disease. Exhaustive studies for tubercle bacilli and for spirochetes were similarly negative.

Johne's disease in cattle has many resemblances to human ileitis in its anatomic configuration, except that the former is regularly demonstrated to be associated with a specific microorganism, the *Mycobacterium johnei*. Williams injected *johnei* subcutaneously into patients with regional ileitis and also into normal controls without establishing any casual relationship between ileitis and Johne's disease. Embson in Denmark described porcine ileitis occurring in swine frequently in more than one of the numerous litters. This disease, which occurs spontaneously in Denmark, has many striking anatomic and histologic characteristics very similar, if not identical, with human ileitis. Tuberculosis was absent. The multiple litter incidence and intestinal fistula formation are common with ileitis as we know it in human clinical material.

A thorough search by veterinary pathologists of the Canadian Government has failed to elicit any trace of a similar porcine disease in Canadian swine (Turner).

small intestine lower and mid ileum by a granulomatous infiltration having all the histologic characteristics of ileitis or of nonspecific granuloma in a Negroess bearing the obvious perineal and vulval lesions of lymphogranuloma. Five lesions were found in the upper and more proximal part of the ileum the lowermost being 6 inches from the ileo-cecal valve. The wall of the bowel was thickened the lumen dilated and the mucosal surface was granular and showed numerous shallow ulcers.

However from this exceptional case of lymphopathia venereum with involvement of the ileum no conclusion can be drawn regarding ileitis as a virus disease at least not as the identical virus of the Nicholas Favre disease. My own attempts to obtain a positive Frei test in ileitis have been unsuccessful. The frequency of recurrences in ileitis even after extensive resections and the inability to demonstrate a specific bacterial agency allow one to maintain an open mind on the possibility of a virus with a predilection for the ileal mucosa. The fact that the two observers did find involvement of the ileum in lymphopathia venereum suggests that a similar though not identical virus may be considered as a possible true etiologic agency in ileitis. More and more as time passes and no positive etiologic agent can be identified the possibility or the probability of a virus agency becomes the more plausible.

Allergy has been suggested by Tallroth as the etiologic agent. He described 2 case histories of ileitis allergica. The finding of many eosinophils in the histologic sections was repeatedly stressed and obviously constitutes the basis for his suggestion. The vascular injury was also typical of an allergic granulomatous process. He regarded the pathologic process in ileitis as a local anaphylactic reaction in the nature of an Arthus phenomenon.

Sarcoidosis

The histologic pathology of Boeck's sarcoid and of ileitis is almost identical. Homans and Hasselstrom stressed the similarity in lymph gland pathology in the two diseases. Longcope and Pierson in their review of sarcoidosis make no reference to intestinal lesions. Williams and Nickerson review 4 cases of sarcoidosis but without any ileal intestinal or colonic involvement. Snapper reviewing the pathology, clinical incidence and histology of the two diseases terms them pseudo-tuberculosis in nature. In their respective clinical manifestations however he differentiates sharply between them considering them unrelated in all aspects.

The findings and implications of Felsen so often quoted in the literature may be variously criticized. The agglutination in the serum of patients against recovered organisms and against type laboratory cultures are today open to the criticism of nonspecificity. The small number of positive stool cultures (10) recovered after an epidemic of acute dysentery is not significant for ileitis.

In our own series of almost 700 cases and in the experience with the additional ward cases at the Mount Sinai Hospital over a period of over 25 years I can recall only 2 cases with a transient positive culture for the Flexner type of dysentery and only an exceptional case with high agglutinations against similar bacteria. In only one instance an agglutination of 1:320 against Hiss was reached.

The imputation that regional ileitis or ileojejunitis is regularly caused by the *Shigella dysenteriae* has not been substantiated and is not acceptable to most authors.

Intruses

The virus of lymphopathia venereum has been suggested as the cause of ileitis. Stafford in 10 cases of lymphopathia venereum found 3 patients suffering from a form of segmental colitis; in no case was the small bowel involved. Because of the cicatrizing tendencies and the possible similarity to cicatrization found in the rectum in lymphopathia venereum, Hoster and his associates carried out the Frei test in 4 cases of resected ileitis and in 2 others of ileitis not resected with negative results. Rodaniche, Kirsner and Palmer considered that the two diseases resembled each other in the primary lymphatic involvement and later development of severe tenosynovial lesions. However in 4 cases of ileitis the Frei test was negative with mouse and human antigens. The serum was also found negative for neutralizing antibodies against the virus. Similar negative results were found by Friedl Meyer. However Llombari and Mavern described a case of lymphopathia venereum with multiple stricture of the ileum as well as a rectal stricture. Ocular manifestations were also present, confirmatory of the virus type of infection. Coultts and Oporo in a study of several cases of lymphopathia venereum were able to demonstrate only one instance with ileal involvement. In this person there was an extensive proctitis and an ileitis involving a large part of the terminal ileum.

Likely and Lutz give a detailed report of an involvement of the

case of granuloma the direct result of an accident such as from an automobile or a fall was ever reported. He makes an exception of course for granulomata resulting from tears of the me enteri from direct violence to the abdomen foreign bodies splinters of wood strangulated hernias and residual suture material. However as early as 1936 Reichert and Mathe cite the case of a man who suffered a stunning blow to the abdomen from the steering wheel of his automobile. Two weeks later he developed severe abdominal pain with vomiting and diarrhea. Later resection of the ileum revealed a granulomatous lesion twelve inches in length which was proximal to and not occupying the usual site for regional or terminal ileitis.

Two cases of regional enteritis following external trauma have been reported from the Mayo Clinic. In one case three months prior the patient had had an accident while horseback riding in which his mount had fallen on him delivering a severe crushing blow to the abdomen. On exploratory operation some weeks later an obstructing lesion was found about 7 feet from the ileocecal valve relief followed a short circuiting procedure. Later the lesion was resected.

The second case involved a farmer who four months previously had been caught between two heavy farm implements sustaining a pulverizing injury to the abdomen. At operation several loops of ileum were bound together by inflammatory adhesions and were fixed to one loop of lower jejunum which was definitely obstructed. The usual edema of the me enteri and enlarged lymph nodes and fistulous tracts so characteristic of ileitis were absent. These cases do not resemble ileitis in anatomic distribution or in symptomatology. They represent true direct trauma to the small intestine with resultant granulomata and obstruction. Nominally they are instances of ileitis of traumatic origin.

Ten Kate in 1936 reported 2 cases of regional enteritis following severe trauma. In one a rupture of the ileum was found at operation though nothing that resembled clinical ileitis the other a characteristic lesion with a fistula from the ileum to the bladder was observed at operation.

Spellberg and Gray cited the case history of a soldier motorcyclist who ran into the end of a stalled truck. Abdominal pain and vomiting supervened within thirty days. X ray revealed a typical jejunitis beginning just below the fœa of Treitz. At operation the jejunum resembled a garden hose being indurated and edematous with accompanying enlarged lymph nodes. Resection of the lesion was eventually required.

More recently isolated sarcoidosis of the small intestine simulating nonspecific ileo jejunitis has been described. This is the first instance in which the real differential diagnosis of ileitis from sarcoidosis involving the small bowel has been verifiably noted though in the literature small intestine involvement has been occasionally suspected. In this paper by Watson and associates 2 case histories are detailed which require analysis. The radiographic picture resembled ileitis or ileo jejunitis. Resected specimens had many of the characteristics similar to those of ileitis except for polyposis; the histologic picture was almost identical. Hadfield in studying 20 cases of ileitis had found 13 in which epithelioid cell tubercles were present and cautiously suggested the identity of ileitis and sarcoidosis.

Moreland has published an article entitled "A case of sarcoidosis of the lung with regional ileitis." A filling defect of the cecum was observed radiographically. At operation resection of the terminal ileum was performed. Typical changes of a sarcoid nature were histologically observed in the removed mesenteric lymph nodes. This case is not convincing as one of ileitis. It could very well however be a good example of involvement of the ileum and colon in sarcoidosis.

The generalized picture of sarcoidosis in all its clinical manifestations including skin and pulmonary lesions and the absence of fistulas, string sign and rectal complication have convinced most authors that the two diseases bear little relationship. The most that can be said is that sarcoidosis may occasionally show involvement of the small bowel. Bernstein, Konzelman and Sidlick report a case of Boeck's sarcoid with true involvement of mucosa of the ileum marked by thickening of the wall with ulcerations measuring 2 x 4 cm. In the case of Lenartowicz and Rothfeld the gastrointestinal tract was diffusely involved. Homan and Has stated that some observers have called ileitis sarcoid of the small intestine. Warren and Sommers collected the reports of 50 cases of sarcoidosis with complete autopsy studies; in 7 of the cases intestinal lesions were described. Three of the cases showed generalized involvement throughout the stomach and bowel; an isolated lesion in the ileum was not described. Twenty one cases of proven sarcoidosis were studied by radiography; in no instance was an abnormality encountered suggestive of gastrointestinal involvement (also Lorber Shry and Wolo hin).

Trauma

Mock (1931) in discussing infective granulomata states that no

fistulous tract to the cecum and adjoining loops of the small bowel. The patient was observed for two years during which time successive diarrhoeal compex and spontaneous resolution. The mass in the deep abdomen disappeared under observation.

The finding of the wax test, while not the cause of the ileitis, was most probably a factor in bringing to light a latent and a symptom of regional ileitis.

Case M.J. A man 25 years of age while in the armed services, was severely injured by the explosion of a bomb on board a U.S. destroyer. Upon recovery he began to complain of abdominal pain and diarrhoea. The radiographic picture upon his discharge was typical of ileitis. Nevertheless he was able to continue in the armed services and obtained an honorable discharge. Under observation, the symptoms of radiographic evidence of ileitis have subsided and his case is considered one of spontaneous cure.

Case C.G. A man in an auto accident was thrown violently against the steering wheel of his car with severe bruises to his abdominal wall. Two months after the injury he developed diarrhoea and abdominal pain and lost 15 pounds in one year. A resection of the terminal ileum revealed a typical regional ileitis. He was well after the operation for 3 years when he again suffered an accident, this time being hit by a streetcar and thrown violently backward. Immediately the diarrhoea recurred. A recurrence of the ileitis in the loop of ileum proximal to the previous anastomosis was suspected though not proven.

In the last ten years we have added 3 more cases wherein trauma seems to have been either an initial factor in the causation of the ileitis or in the aggravation of a possibly pre-existent disease. In one case a violent fall upon the abdomen immediately preceded the onset of symptoms. In 4 of other cases an automobile collision usually of the head-on type immediately preceded the initiation of symptoms and seemed scientifically and logically to be responsible for the causation or aggravation of the intestinal disease. In another case of quiescent ileitis the fracture of a finger was immediately followed by a recrudescence of all intestinal symptoms. With the increasing number of automobile collisions particularly of the head-on variety the question of the relationship of traumatic intestinal diseases comes more and more to the foreground. In a head-on accident the body of the driver is violently catapulted forward the lower thorax and the abdomen striking the steering wheel. The subsequent development of abdominal symptoms raises both the point of the origination of a visceral disease and of the aggravation of

In my own experience in spite of initial skepticism there seems to be sufficient basis for associating trauma and ileitis in the relationship of cause and effect (Crohn). This conclusion is based upon experience with the following six cases briefly abstracted

Case 1 S 4 A man 39 years of age in an automobile accident was violently thrown forward against the steering wheel of his car sustaining severe abdominal trauma. Abdominal cramps and diarrhea supervened almost immediately though the man had previously always been well. Operation performed less than two weeks later because of the severity of the complaint revealed a typical terminal ileitis cured by resection. The patient received a large award from the courts. This was my first experience of that type as an expert I testified against the likelihood of trauma creating such a lesion as ileitis though I was unable to deny the probable aggravation of a pre-existent latent lesion. My viewpoint was changed by the succeeding experiences.

Case 2 J 4 A boy 17 years of age always previously well was thrown violently across the aisle of a bus as it was involved in a collision striking his abdomen on the forward seat. He immediately developed hematemesis and symptoms of a traumatic duodenal ulcer. A gastro-enterotomy was performed a few weeks later the stoma functioned badly. At re-operation a typical regional ileitis was noted and resected. It seems reasonable to deduce that both the duodenal ulcer and the ileitis which involved the terminal loops of the small bowel were traumatic in origin.

Case 3 W W A 26 year old man suffered at 3 years of age a profound trauma when struck by a moving truck. The child immediately developed an abscess in the right lower quadrant of the abdomen requiring several operations and characterized by an obstinate fecal fistula to the abdominal wall. When he was 8 years of age the previously closed fistula reopened spontaneously and remained open for several months. Four years later the fistula again reopened but closed without surgical intervention. The same sequence of events took place four years ago. For the last ten months the patient has presented the typical symptom of regional enteritis with diarrhea and abdominal pain. Two fecal fistulas are present on the right abdominal wall.

Case 4 H 1 A woman 50 years of age lifted a heavy object and immediately felt a pain in the right lower quadrant of the abdomen. She suffered no diarrhea or fever. Seven weeks later on physical examination a tender sausage-shaped mass was noted in the right lower quadrant of the abdomen. Radiographs also a clear picture of ileitis was seen involving 1 to 18 inches of the terminal ileum with severe short

several such striking examples are of such interest as to merit closer analysis.

In 1934 the first instance of ileitis occurring in sibling was published. A boy of 14 who represented historically a very early clinical history of ileitis was resected and the diagnosis firmly established. Two years later his 32 year old sister complained of abdominal pain and vomiting and developed signs of intestinal obstruction. At operation a typical ileitis involving the terminal 8 inches of small intestine was resected. The anatomic situation and pathologic attributes of the lesion were identical in both siblings.

In this present study we have encountered 12 instances of familial involvement.

REGIONAL ILEITIS	
<i>Relationship</i>	<i>No. of Cases</i>
Brother and brother	2
Brother and sister	3
Mother and son	2
Mother and daughter	4
Father and son	1

In two other brothers one had ileitis resected the second was a case of typical ulcerative colitis. Mother and daughters constitute a different group which was seen four times all the cases being confirmed. In another instance the mother had ileitis the daughter ulcerative colitis. In a fourth instance the child had ileitis and the mother and two maternal aunts of the child had ulcerative colitis. We have again noted an uncle suffering with ileitis his niece with segmental or right sided colitis.

Three family groups further afford a striking picture. In the first a young woman her brother and her half brother all have ileitis the father is suffering from ulcerative colitis. In the second family group we note ileitis segmental colitis and ulcerative colitis in 3 adult siblings (fig. 1). In the third family group a child and her two aunts by consanguinity have all had ileitis confirmed by operation. Bockus refers to two cousins suffering with regional ileitis with extension into the colon ileocolitis both resected and well they had previously lived together in the same house. Brown and Schiefel have reported regional enteritis affecting 3 siblings 2 sisters and one brother. In 2 of the siblings the colon was involved as well as the terminal ileum. A case of regional

a pre existing disease. This type of accident applies with some reason in instances of low grade ileitis and such cases are becoming increasingly common in the courts.

Ileitis is a disease of great chronicity often latent for years. In the analysis of case histories in general it is not unusual to read of mild almost negligible occasional complaints for 5, 10 or 20 years before the eventual diagnosis is established. Nor is diarrhea a constant clinical symptom in ileitis or enteritis. The thought seems therefore justifiable that in these instances where trauma has been related to ileitis actually one is dealing with an aggravation of a pre-existent latent ileitis. However the cases from the Mayo Clinic and the first 3 cases in my personal experience seemed sufficiently well checked and proven to allow the inference that the trauma preceded and caused the intestinal lesion. In the other cases the aggravation of the lesion by the trauma seems justifiable.

Traumatic enteritis in its clinical course is identical with ileitis as we know it in its well recognized forms. Abdominal mass, fistula formation, diarrhea and fever are all present. Segment other than those of the terminal ileum are more likely to be affected by the indiscriminate application of the trauma.

Spontaneous resolution was twice observed, an incidence that would seem higher than in the control nontraumatic cases.

In discussing the relationship of trauma to intestinal diseases, Linger and Molineus have laid down the following four dicta:

1. It must be shown that no prior disease had existed.
2. The trauma must be sufficient to act as a possible causative factor.
3. The active symptoms must follow directly upon the trauma.
4. The clinical symptom must be identical with that of the disease (Brahdy and Kahn).

In most of the quoted case of trauma followed by symptoms of ileitis the four dicta have been truly fulfilled.

Familial Incidence of Ileitis as a Possible Etiologic Factor

Ulcerative colitis non-specific, a sister disease rarely occurs in more than one member of a family. My own experience and medical literature in general bear out that fact. On the other hand regional ileitis or enteritis occurs in multiple instance in intimately blood-related members of a family sufficiently often to warrant attention because herein may lie a clue if not to etiology at least to familial predisposition. My note on

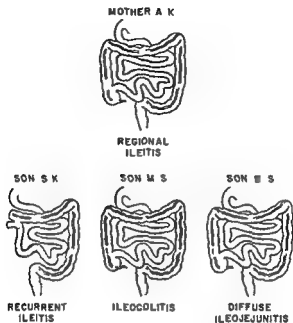


FIG 2 Familial incidence in one family

of ulcerative colitis one could understand contact infection such as occurs in epidemics of bacillary dysentery or in amoebiasis by finger transmission or by insects particularly flies. Or one could conceive of a common vector. Since such a specific etiologic agent is not known it seems more logical to fall back upon at least a familial predisposition to the unrecognized infective agency such as factor predisposing to ileitis to ulcerative colitis or to both diseases. The mixed cases of ileo-colitis seen in this series again only draw attention to the common liability of small and large intestine to the offending agency or agencies.

*Theories Regarding the Pathologic
Mechanism in the Creation of Ileitis*

Most of the hypothetic considerations regarding the actual location of the lesion and the possible direct physical factors in initiating the granuloma have centered about the terminal ileum and ileocecal valve. This viewpoint ignores the fact that the lesion may occur at any level of the small intestine and also that recurrences of ileitis occur far from

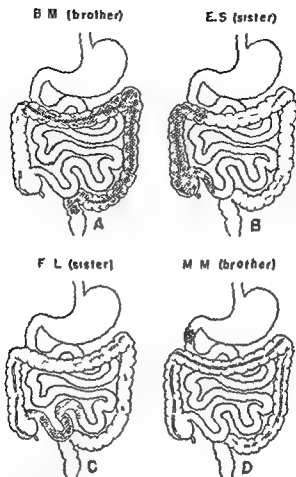


FIG 1 Familial incidence of various findings

A Ulcerative Colitis B Segmental Colitis (right-sided) C Regional Ileitis D Duodenal Ulcer

ileitis in a father and on his also been described. Heard and John cite a more recent case of chronic ileitis in a mother confirmed by exploratory operation. Two years later her child 7 1/2 years of age was operated on for an acute ileitis.

The significance of the findings remains conjectural; they are too interesting however to be dismissed without consideration. If a proven bacterial or viral agency could be incriminated as the cause of ileitis or

compromised by undergoing rotation Bell however in experimental studies could not reproduce granulomata by interference with the blood supply

The Theory of Lymphatic Block

Of much greater interest is the question of the relationship of the mesenteric lymph glands and the lymphatics of the intestinal wall to granulomatous ileitis. The constant finding of enlarged lymph nodes in the mesentery of the affected loops of intestine while easily explained on the basis of secondary infection has caused some writers to advance the hypothesis that the primary lesion may be resident in the lymphatic tissues the organic changes in the wall of the gut being secondary thereto. Holman in discussing a paper by Bell in 1934 asks whether the lymphatic hyperplasia is an expression of a chronic infection originally in the bowel or possibly the primary lesion with subsequent fibrosis and secondary constriction of the intestinal canal. Two years later Reichert and Mathes published a paper on Experimental lymphedema of the intestinal tract and its relation to regional cicatrizing enteritis. The dominant features of the intestinal lesion in ileitis resembled a low grade infection with a concomitant chronic lymphatic obstruction and edema. They observed the pathologic resemblance to elephantiasis as seen in the extremities of the body. In animal experiments sclerosing substances were injected with a fine needle into the mesenteric lymphatics and serosal lymphatics of the wall of the intestine.

The material used for sclerosing purposes included crystalline silica mesh bismuth oxychloride indelible lead or sodium morrhuate. In some animals a 24 hour broth culture of *B. coli* was given intravenously one to three hours before the lymphatic injection, those bacterial injections occasionally being repeated at intervals subsequent to the acute experiment. When the animal was killed the treated segment of bowel felt thickened, some of the mesentery lymphatics were dilated, some sclerosed, free peritoneal fluid was not present. The thickened bowel wall showed inflammation and thickening of the serosa, edema of the circular and longitudinal muscle fibers, the submucosa was swollen and infiltrated with leukocytes, the mucosa swollen but not ulcerated. Chronic pathologic changes persisted without subsidence for months after even a single sclerosing injection. The changes were seen in all specimens (12) examined but were most marked in those experiments in which bacterial suspensions were intravenously injected coincidentally.

the original site of inflammation and from the valve of Bauhin. Naturally the first suspicion was directed at the appendix as a causative factor. Many writers have suggested that a fibrinoplastic process beginning in the appendix extended to the ileum thus constituting terminal ileitis (Lowen). Fischer made the same claim but this time through the mediation of the mesenteric lymph nodes. Ravdin and Rhoads again pointed out the similar pathologic changes in fibroplastic appendicitis and the chronic stage of regional ileitis. Homans and Hass and Erb and Farmer suggested primary appendiceal disease as an etiologic factor.

In refutation of this idea it should be noted that the appendix had previously been removed in over 25 per cent of cases of ileitis. The life course of the disease is in no way altered or stayed. The resected appendix apart from showing slight chronic changes of the usual type seen in adult life is free of typical granulomatous changes such as characterize *granulomata* and *ileitis*. In this series we encountered only six instances of gangrenous appendicitis either during the active phases of the disease or subsequent to short circuiting procedures. Nor is there reason to expect the appendix to be involved in ileitis since the appendix originates from the base of the cecum beyond the ileo-cecal valve and is separated anatomically from the ileum by the ileo cecal valve which is such an efficient barrier in preventing the spread of the ileitis to the cecum. Nor does acute appendicitis occur more frequently in the combined cases with cecal involvement. Histologically the appendix in the resected specimens of combined ileocolitis does not participate in the peculiar and characteristic granulomatous inflammation.

Vascular Changes

The analogy of ileitis with intestinal granulomata might well suggest that the similar pathologic picture in both diseases results from an identical impairment of the blood supply. Those authors who have written on the subject of granulomata of the intestinal tract have emphasized volvulus, intussusception, strangulated hernia and traumatic rents as direct causative agent leading to granulomatous mass formation. Ginzburg and Oppenheimer⁹ particularly stress the reduced vascularization that results in mucosal necrosis, ulceration and secondary hyperplastic granulomatous change. Barbour and Stokes mentioned the possibility of a chronic recurrent intussusception. Bockus and Lee discussed the peculiar blood supply of the terminal ileum and its mesentery suggesting that the terminal branch of the ileocolic artery might be

The possible relationship of acute mesenteric lymphadenitis to acute and chronic regional enteritis presents an interesting thought. Jackson suggested the kinship of the two diseases. However, in 15 cases he found only a mild hyperemia of the terminal 3 to 4 inches of the terminal ileum; he has no record of any case of ileitis originating in or from mesenteric lymphadenitis. Rocky noted thickening of the ileum in children with acute mesenteric lymphadenitis in 4 cases. All were valid cases of acute ileitis with marked lymphadenopathy, and this in September 1932, before the first publication on ileitis.

On the other hand, Eliason and Johnson state that they know of no case of acute ileitis originating in acute mesenteric lymphadenitis. In the 15 case of acute ileitis observed by them and operated on, they found no intraperitoneal picture that resembled acute mesenteric lymphadenitis; either a regard abundant free peritoneal fluid or massive disseminated lymph gland enlargement.

In 1932, Strombeck published his observations on 40 cases of acute nontuberculous mesenteric lymphadenitis controlled by operation. In 22 instances, he noted the occurrence of acute terminal ileitis, which he presumed was the point of origin of the infection. Ten to 20 to 30 cm of terminal ileum proximal to the ileo-cecal valve were involved, the intensity of the affection being at the valve and diminishing upward. The Feyer's patches were large and grainy, boat-shaped swellings. The greatest frequency occurred between the ages of 5 and 15 years, corresponding to the greatest frequency of acute ileitis. Strombeck distinctly states that in the follow-up covering at least 4 years, he has never seen any such case develop into the picture of a chronic regional ileitis. Of 31 cases of nontuberculous mesenteric lymphadenitis observed by Erskine, 10 showed some involvement of the ileum in an inflammatory process associated with large hypertrophied lymph nodes in the mesentery. He does not relate the disease to true regional ileitis. In his opinion, the lymph nodes are first involved and then the appendix or the ileum or both by an extension of the process.

The observations of Strombeck more or less dispose of the hypothesis that chronic regional enteritis begins as an acute mesenteric lymphadenitis. The largest percentage of cases of ileitis in this series were chronic in nature throughout their course. The abdominal finding at operation in acute mesenteric lymphadenitis: generalized enlargement of mesenteric lymph nodes, much clear fluid, occasional involvement of terminal ileum. In acute ileitis, one observes scant free fluid, edematous engorgement of

with the lymphatic block. The intestinal lymphedema was found to persist as long as ten months without any evidence of subsidence.

It is interesting to note that Poppe using similar method of lymphatic injections claims to have produced ulcerative colitis in dogs by obliteration of intestinal lymphatics. However Sznajko and Necheles repeating their work not only failed to produce ulcerating lesion in the colon of dogs but point out in contradiction to the results of Reichert and Witte that the lesion in the colon showed a tendency to rapid disappearance and no tendency to chronicity. Chess et al carried out extensive experiments on 37 dogs and 12 rats using sand and talcum as sclerosing elements injected into an isolated loop of ileum and cecum. Marked lymphoid hyperplasia of the small bowel was experimentally produced by forced feedings of sand and talc the animals died of plastic peritonitis some of them with granulomas of the liver. The intravenous injection of live bacteria in addition to the mechanical effects of the sclerosing substances resulted in ulcerations of both large and small bowel.

It had already been suggested (Probstein and Gruenfeld) that normally the flow of the intestinal content is retarded at the ileo-cecal valve the lymphatic tissue in the mucosa and submucosa is here more abundant than in the segments of the bowel a factor which enhances the likelihood of bacterial absorption. Studies on the ileo-cecal junction (ileo-cecus) by Barger and associates demonstrated longitudinal muscle fibers entering the labia of the valve for a considerable distance and meeting at the crest. Gelatin solution injected at the cecal mucosa were blocked at the tip of the labia similar injection made on the ileal side in 15 cadavers were also blocked at the valve. Obviously there is a lymphatic blockage at the tip of the labia of the ileocecal junction.

Several workers particularly of the English school (Frazer) have considered as an etiological factor some local disturbance in fat metabolism or some fault in intestinal lipid absorption a being involved in the characteristic tissue reaction of ileitis¹. Hirsch has pointed out that fatty acids in the body produce foreign body giant cell reactions. Cooke in his reflections on steatorrhea and regional ileitis states "To sum up the view is put forward that regional ileitis is the result of tissue reactions to the breakdown products of lipid complexes or possibly other metabolites or ingested substances leading to further defects in the absorptive powers. The process may be temporary or persist and aggravate the lesion already present."

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the terminal ileum and only localized lymph node involvement. Perforation of the acutely inflamed ileum with localized walled off peritonitis is not unusual.

Age and Sex in Regional Ileitis

In our series the age distribution at onset of symptoms is shown in table 1.

TABLE 1
AGE DISTRIBUTION AT ONSET OF REGIONAL ILEITIS

Years	Number of Cases	Incidence (%)
1-10	16	3.0%
10-20	130	24.5%
20-30	67	39.0%
30-40	117	22.0%
40-50	37	7.0%
50-60	16	3.0%
60-70	7	1.3%
<hr/> Total		130

The average age at onset was 27.6 years. The maximum incidence falls between 20-30 years though adolescence is well represented. Childhood and old age are scantily represented. The oldest case was 74 years of age the youngest case was 9 months in one instance and 2 1/2 years in another. The 9 month old case was confirmed by operation and by x-ray studies.*

TABLE 2
AGE INCIDENCE IN REGIONAL ILEITIS (RAYDIN AND JOHNSTON)

Age Group	Number of Cases	Percentage
1-10	18	4.7
10-20	68	17.8
20-30	140	36.6
30-40	76	19.9
40-50	40	10.4
50-60	4	6.2
60-70	13	3.4
70-80	3	0.8
<hr/> Total		322

A case of ulcerating enterocolitis in a newborn has been described in the literature (Kemp, Perlongiero and Wein).

These figures compare favorably with those of other authors who have collected a large series of cases. Thus Strombeck collected from the literature 91 cases; the greatest incidence (40 cases) fell between 20-30 years of age or 44 per cent agreeing almost identically with figures in this series. Similarly Ravdin and Johnston in a collection of 393 cases from the literature give the age incidence as shown in table 2.

At the Mayo Clinic (Von Patter) the age of patients at the onset of symptoms (table 3) of regional enteritis was as follows:

TABLE 3

<i>Age at Onset Years</i>	<i>Patients</i>
4	2
5-10	21
11-15	62
16-20	103
21-25	116
26-30	113
31-35	66
36-40	34
41-45	37
46-50	21
51-55	11
56-60	4
61-65	6
66-70	1
71-74	3
Total	600

Males predominate over females in their susceptibility to the disease. In the present series there are 306 males and 236 females involved representing a proportion of 56.5 per cent males to 43.5 per cent females. These figures again agree with the mass compilation of cases from the literature in which males constituted 56.6 per cent of the cases (Ravdin and Johnston). The figure given in earlier years based on a smaller group of cases (Crohn) of males predominating over females in a proportion of 2 to 1 is not borne out when large group statistics are invoked.

Schiff garnered the statistics from the literature on 48 cases of ileitis in childhood. The ages varied from 13½ years to 16 years as shown in table 4.

TABLE 4
AGE INCIDENCE OF ILEITIS IN CHILDHOOD (SCHIFF)

<i>Age</i>	<i>Number of Cases</i>
13½ years	1 case
2 3 years	4 cases
4 6 years	6 cases
7 9 years	18 cases
10 12 years	5 cases
13 14 years	7 cases
15 16 years	7 cases
<hr/>	
Total	48 cases

He emphasized particularly the acute phase of the disease in childhood and the similarity of the clinical picture to that of acute mesenteric lymphadenitis.

Psychosomatic Factors

Since ulcerative colitis has been generally accepted as one of the so-called psychosomatic diseases the question has been raised: Is ileitis also caused by or subject to psychic factors? In the literature the views vary but in general there is little support for such a consideration. As early as 1930⁹ Blackburn, Hadfield and Hunt studied 22 consecutive cases of ileitis in a control group but could find no psychological characteristics in the ileitis cases. Rokus found few phlegmatic individuals in ileitis patients; most of them were extremely sensitive and excitable, some even manifesting severe psychoneuroses. More recently (1951) Dashiell and his group noted some emotional distress in a majority of their 40 cases of ileitis. Ingelfinger grouped both ulcerative colitis and ileitis patients as psychiatric problems and economic failures in contrast to the more stable and aggressive peptic ulcer individual. Paulley reported 4 cases with unusual dependence. Blackburn 4 anxiety states in 22 cases.

It is interesting to note that in the large collection of 600 cases reported by Von Patter and his group from the Mayo Clinic no mention is made of psychic factors as influencing the course of the disease. Crockett in 16 routine psychiatric examinations of cases of ileitis found no substantial support for the suggestion that emotional stress is a major etiologic factor.

My own experience does not in any way support the concept of ileitis as a psychosomatic disease. The 700 patients we have seen have

been no more — no less emotionally unstable than a mass of control individuals. When one considers that in the office practice of an internist 80 per cent of the cases seen are functional, then the ileitis case by contrast in spite of his severe organic symptoms seems temperamentally quite stable. True many cases of ileitis have been — cued from psychiatric institutions but that is only because the diarrhea was regarded as nervous and the true source of the illness was completely missed. The debilitating effects of the organic symptoms and the associated anxiety eventually break down the most complete self-control. The older age groups of ileitis cases are remarkable for their fortitude and stamina in spite of low grade symptoms covering long periods of years — nor — there anything to approach the ebullience and self sufficiency of a healed case of ileitis (postoperative) even though a recurrence of his illness catches up with him 19 or 25 years later. Among the 500 cases recorded in Canadian hospital in a recent five year period (Turner) many of the cases were farmers and urbanites — no particular category of personalitie could be discerned.

We know of no single illustrative case where the onset of ileitis was associated with or could be attributed to psychic traumatic situations. Nor can we attribute recurrences of the disease postoperatively to any psychic factors. Many recurrences take place 11 14 17 19 or even 25 years after the original operation and it is difficult to conceive a former patient who survived the vicissitudes of life over all those years falling prey to a recurrence of ileitis merely as a result of a more unusual set of adverse psychic factors.

An interesting instance of both psychic strain and physical disease as the background for the etiology of regional ileitis is seen in the following case:

H B S rral No 20 mal ag 29 years Iati m eul ted i the U S Army n 1939 se ving in the Philippine Islands. He was a prisoner of war f om 1942 t 1945 on of the many who part c pated n the Death March f m C reg dor. He uffe d from b cillary dysentery ameb o dv ntery und lant fever malaria pellagra acurvy ber beri and seve e malnut tio. Dur ng all this t me he had severe d arrhea. In July 1945 the d gno s of r gional ile t s was made by x ay e aminat on the g anulomato s p ocess involv g the whole of the ileum. When seen in 1946 h had recove ed weight and strength and was well except for the d a rhe a. X r y xam nation demon trated a no mal colon but a severe d ffuse eg on l ileit. The s gm doscopy wa n g t ive.

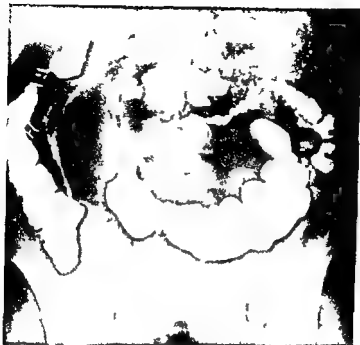


FIG. 3 Regional ileitis in a man who survived the Death March and three years in a Japanese concentration camp

Social Status Race Nationality Religion

All classes of society are affected equally by ileitis: private hospitals and public wards seem equally represented in proportion to population. Bockus appears impressed with the failure to encounter regional ileitis in families who have been in the upper economic brackets for one or two generations. All races and climes seem represented in this disease since the literature from all over the world contains publications of cases (Africa India Sweden Puerto Rico East Africa South America). Bockus again mentions the fact that no cases had been reported from Latin America or from Cuba: this deficiency has since been supplied (Fermin also Valencia Parpacen). He also observed a preponderance of cases from the southern sections of South America. In 1944 there were 134 admissions from ileitis in the total U.S. Army; in 1945 there were 145 similar admissions for the entire Army. The corresponding rate per

1000 strength for each year is 0.2%. Kieffer found that regional ileitis occurred 70 times in 100 000 registrants at the Lahey Clinic.

As regards race a greater incidence of the disease among the Jewish race was first suggested by Homans and Hass. In the experience of Bockus 13 of 21 cases were Jewish, thrice the normal expectancy of the disease for the sample from which the cases were drawn. However in Marshall's series at the Lahey Clinic only 3 of 29 cases were Jews. Ashley at the Harper Hospital in Detroit found only 8 of 31 cases in his series to be Jews. Brown and Donald 26 per cent Jews (Mayo Clinic). The study comprising 22 cases of ileitis in the records of the Binghamton City Hospital and other hospitals in Broome County, New York, include no cases involving Jewish patients (Sneitson and Ryan). Negroes, Orientals and Latin Americans are all represented and reported in the literature. One of my own cases was a Hindu from British India. Strombeck of Stockholm with 26 cases reported and with an extremely careful analysis of etiology fails to mention race or social position.

Personal communication

Chapter 3 Gross Pathology

Gross Pathology

REGIONAL ILEITIS is a nonspecific granulomatous inflammation of the ileum involving most frequently the terminal segment or segments of the small bowel. In gross appearance it has definite characteristics that distinguish it from granulomata elsewhere in the alimentary tract these specific features being most pathognomonic when the terminal ileum alone is involved. The histologic microscopy of the disease is nonspecific it is not to be differentiated from other granulomata from sarcoid and (often only with difficulty) from tuberculosis.

In our series of 542 cases the extent of ileal invasion was noted in our records in 511 instances. The inability to state the amount of anatomic involvement in the remaining cases was due to the fact either that they had been previously operated on elsewhere or that no surgical corroboration of the radiographic picture had been obtained.

The anatomic distribution in this series is shown in table 5.

TABLE 5
ANATOMIC DISTRIBUTION IN REGIONAL ILEITIS (Fig. 3)

Distal (inches)	Cases
12	272
24	167
2-3 (feet)	55
3-4 (feet)	13
4-6 (feet)	47
Mid ileum	7
Total	511

In one remaining case the terminal ileum and the uppermost ileum were discontinuously involved. The predominance of the lesion limited to the terminal 12 inches of ileum is noteworthy the next longest group not only involves the terminal segment but extend continuously to cover the distal 24 inches of ileum the smallest group involves the terminal and all of the upper reaches of the ileum which we arbitrarily indicate as being about 6 to 7 feet in length from the ileocecal valve.

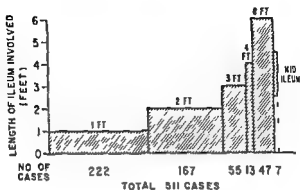


FIG 4 Anatomic distribution of pathologic lesion (cases) ileo cecal valve to transition between ileum and jejunum

In the series reported by Blackburn Hadfield and Hunt of 22 cases the terminal ileum was involved in 19 instances the distal ileum in 3 instance. In 6 cases the cecum was involved in an analogous extension of the process. The length of ileum involved varied between 4 and 60 cm with an average of 19 cm ($7\frac{1}{2}$ inches).

Why the terminal ileum is so often the sole seat of the disease and apparently the oldest and parent lesion in the process is difficult to explain. Most general diseases of the small bowel are located at or near the terminal ileum just proximal to the ileo-cecal valve. These include benign and malignant new growths foreign body granulomata primary and secondary hyperplastic tuberculosis sarcoid carcinoid and endometriosis. The normal narrowing of the lumen of the small bowel as it progresses distally is maximum just proximal to the valve of Bauhin the valve itself constitutes a mechanical device for slowing up the progress of the column of chyme the lymphatics of the intestinal wall particularly the mesenteric lymph nodes are in their greatest density at or about the ileo cecal angle. The natural blockage of the lymphatic drainage at the labia of the valves as shown by Bargen et al localizes an infection proximal to the valve and discourages or prevents in the largest percentage of cases the transition or extension of the disease to the cecum. Occasional cases are cited where the lesion involves a very short segment of ileum proximal to the valve without involving the actual terminal segment of the ileum but these cases are exceedingly rare.

The gross appearance of ileitis as seen at the operating table

Chapter 3 Gross Pathology

Gross Pathology

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The anatomic distribution in this series is shown in table 5.

TABLE 5
ANATOMIC DISTRIBUTION IN REGIONAL ILEITIS (FIG. 3)

Distance (inches)	Cases
1	7
24	167
23 (feet)	55
34 (feet)	13
46 (feet)	47
Mid ileum	7
Total	511

In one remaining case the terminal ileum and the uppermost ileum were discontinuously involved. The predominance of the lesion limited to the terminal 12 inches of ileum is noteworthy; the next longest group not only involves the terminal segment but extends continuously to cover the distal 24 inches of ileum. The smallest group involves the terminal and all of the upper reaches of the ileum which we arbitrarily indicate as being about 6 to 7 feet in length from the ileocecal valve.

to separate the loops it will frequently be noted that they are adherent because of fistulous communications or fistulous tracts originating in the porous terminal ileum extending through the mesentery to the adjoining loops of small or of large bowel. Occasionally a slow walled off perforation of the terminal loop of ileum will be observed covered over by a plastic exudate and sealed off by neighboring viscera usually another loop of ileum or the sigmoid. Bockus emphasizes that there is a close relationship between the destructive changes in the mucosa and the extent of covering of the serosa with mesenteric fat. The termination of the mesenteric fat on the antimesenteric portion of the serosa corresponds to the line of demarcation between diseased and normal mucosa.



FIG. 6 Characteristic appearance of lesion on regional ileitis involving terminal ileum and segmental lymph nodes

After the resected specimen is opened one notes the edema and thickening of all the coats of the bowel (figs 5-6). The lumen of the bowel itself is reduced and compromised by the swelling of the walls until the actual lumen is reduced to a cordlike stenotic opening. This reduction of the lumen of the bowel in old chronic distal ileitis accounts for the characteristic "string sign" seen in radiographic films. The process may continue to true stenosis with intestinal obstruction and proximal

or as studied in the resected specimen is that of a brilliantly red congested edematous mass—solid and firm resembling a rubber hose or as Dalziel has described it 'an eel in a state of rigor mortis'. An equally apt description is that of Jackson who likened the diseased segment to 'a dead water soaked night crawler'. The serosal surface is greatly injected usually covered by fibrinous exudate the lumen of the gut may be dilated or in the end stages reduced to a narrowed cordlike tube. The extent of involvement is manifest by the varying degrees of hyperemia the engorgement of the vessels the serosal exudate and the gross enlargement of the accompanying mesenteric lymph nodes. The hyperplasia of the mesenteric lymph nodes parallel the extent and degree of the inflammatory lesion. Where the lesion ends usually more or less abruptly the serosa of the proximal bowel appears normally shiny and smooth and the obviously enlarged mesenteric nodes are no longer visible.

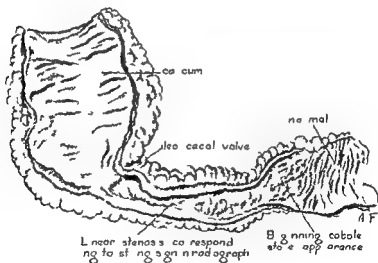


FIG. 5. Characteristic lesion in resected specimen typical regional (terminal) ileitis basis of string sign.

The mesentery of the involved bowel is boggy swollen and visibly thickened. Usually one or more loops of small intestine are matted together forming a palpable inflammatory mass. If an attempt is made

tion on a pathologic basis seems amply verifiable. The first or localized group may and does progress to stenotic fibrosis, remains stationary and may lead to intestinal obstruction. They lend themselves favorably to surgery. The second group is scattered, progressive in the nature of a mucosal or submucosal lesion, less well defined anatomically, with less involvement of regional lymph nodes and less amenable to accurate definition during exploratory operation. This mucosal or submucosal type explains to a large degree the disappointing end results of surgical intervention.

Microscopic Pathology

There are no specific features that characterize or are pathognomonic of ileitis in contrast to granulomata or so-called pseudotuberculous diseases in general. The histologic sections show varying degrees of acute, subacute and chronic inflammation, predominantly marked by infiltration of polymorphonuclear leukocytes, plasma and round cells and fibroplastic elements. The earliest lesion is apparent in the submucosa where the intensity of the lesion is greatest (Hadfield, Schepers). Several observers have agreed in regarding the submucosa as the original site of the onset of the disease process. The more superficial necrosis and ulceration of the mucosa is the result of inflammatory arteritis and phlebitis of the underlying vascular supply. The mucosa is dequamated, the architectural structure of the glandular tissue is destroyed and replaced by plasma and round cell infiltration. In the late stages of the disease the inflammatory reaction is more focal in character, covered on the mucosal side by nodular thickening reminiscent of tubercles. The enlarged, congested skeins of inflamed lymphatics are often apparent even through the thickened serous peritoneal covering. Mallory made much point of the fact that he found large and numerous endothelial leukocytes lying free and blocking the lymph spaces as well as lying in the interstitial tissues. These cells are flat and polygonal with granular eosinophilic cytoplasm and hyperchromatic nuclei. The reaction is sharply focal and intervening stretches of the lymphatics show dilation. These same findings have been confirmed by the histologic studies of Rappaport, Burgoyne and Smetana.

Microscopically the presence of giant cells is very striking. In the vicinity of the giant cells one often sees groups of pale cellular structures resembling vegetable cells in nature. The giant cells are not specific to ileitis; they had been noticed previously by Moichowitz and Wilensky.

dilatation of the bowel loops the stenosis being due to cicatricial contraction of old inflammatory scar tissue at the site of the ulcerating lesions

The mucous membrane has a cobblestone appearance due to the fact that the transverse folds of the mucosa are in part destroyed and are intersected by deeply grooved longitudinal ulcerations that extend through the length of the specimen. These longitudinal ulcerations are deepest along the mesenteric border of attachment it is in this area along the mesentery that the sinus and fistula tracts emanate. The surface of the mucosa is superficially desquamated the markings are gone deep ulcers 0.5 cm to 1 cm in diameter are interspersed between areas of proliferated almost polypoid hyperplastic mucosa. True polypoid formation in late cases as seen in ulcerative colitis is frequently observed. The submucosa is markedly thickened edematous and congested the muscularis is thickened and hyperplastic the serosa its sheen gone is bright red many times its normal thickness in depth and covered by exudate (Otani)

The gross lesion in the bowel wall terminates rather abruptly a sharp line of demarcation is lacking but the mucosa within one or two inches of the proximal area of involvement will suddenly lose its edema and thickening and shortly resolve into normal mucosa. Unfortunately the inflammatory process has a tendency to extend proximally by kangaroo like jumps skip lesions of involvement are common proximal to the distal involved segment these skip lesions being separated by skip areas of normal mucosa. The extent of the skip may vary from a few inches or in multiple skip lesions to several inches up to 2½ feet between the parent and the skip lesion. Occasionally one sees isolated skip lesions from terminal ileum to mid jejunum and even to duodenum itself.

In older phases of the disease the exudative or inflammatory reaction is replaced by a fibrostenotic process the mucosa appears atrophic with occasional superficial erosions and islands of papillary or polypoid hyperplasia. The lumen of the gut may be so reduced as barely to admit a large probe. In advanced cases extensive inflammatory polypoid formation is visibly evident and is readily demonstrated by radiography.

Pemberton and Brown have made an important contribution in differentiating the lesion in ileitis into two categories (1) involvement of a shorter or localized segment of the ileum a single lesion (2) a similar process which involves large segments usually multiple with a greater tendency to progressive extension. Clinically this differentia

tion on a pathologic basis seems amply verifiable. The first or localized group may and does progress to stenotic fibrosis, remains stationary and may lead to intestinal obstruction. They lend themselves favorably to surgery. The second group is scattered, progressive in the nature of a mucosal or submucosal lesion, less well defined anatomically, with less involvement of regional lymph nodes and less amenable to accurate definition during exploratory operation. This mucosal or submucosal type explains to a large degree the disappointing end results of surgical intervention.

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FIG 7 Pseudo tubercle with epithelioid cells arranged in a whorl around giant cells in submucosa (Regional ileitis)

in their study of intestinal granulomas and were thought by them and by subsequent writers to be due to foreign body inclusions vegetable matter or lycopodium spores. Homans and Hass thought the giant cell to be a reaction to lipid material Reichert and Mathes to possible silica or talc inclusions. This vegetable material becomes entrapped in the deep mucosal ulcerations enters the lymphatics and becomes encapsulated in the process of healing. The attempts of earlier authors to include ileitis as a form of tuberculosis was probably due to the findings of giant cells of the Langerhans type. Warren and Sommers were able to reproduce the disease by sclerosing substances and by the injection of lipid materials. They also observed that two specimens removed from cases of regional ileitis contained colorless rounded objects with smooth surfaces. They were doubly refractory and polarized light.

Hadfield has made an intensive histologic study of 20 resected specimens at St Bartholomew's Hospital in London. He particularly emphasized the early and intense involvement of the submucosa considering that the mucosa was probably secondarily involved in the process of extension and also by necrosis due to vascular infiltration. The early



FIG 8 Lymph node showing pseud tubercle formation with giant cell system

changes in the submucosa consist of hyperplasia of the lymphatic tissue and obstructive lymphedema. The submucosal hyperplasia and early and extensive involvement of the lymphatics occurs in his experience in 95 per cent of the cases. These early areas of lymphadenoid tissue show clear evidence of cellular activity with a central zone of proliferating reticulum cells surrounded by a narrow zone of lymphocytes (figs 8-9). A specific response occurs. The affected germinal centers become replaced by proliferating endothelial cells. A Langerhans giant cell can usually be found at the center of the nodule. The follicle now becomes a giant cell system. Hadfield states that in the several hundred sections he has examined caseation has never been observed. The typical specific reaction with giant cell inclusions characterized the sections of lymph nodes found in the mesentery and accompanying the specific lesion in the gut (figs 9-10).

Actually, Hadfield found giant cells in 13 out of 20 cases examined. Necrosis within the granulomatous areas in the ileum or in the lymph nodes rarely occurs; caseation never. In the series of Warren and Sommers, necrosis was observed in 8 of 61 cases (13 per cent). Refer

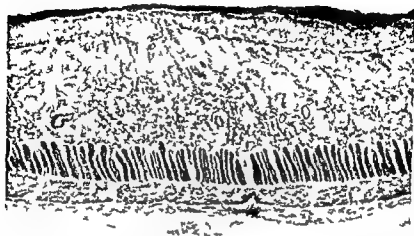


FIG 9 Longitudinal section of lip lesion. Marked submucosal thickening due to granulomatous infiltration. Epithelium completely ulcerated and surface covered with a purulent exudate.

ence has been made to the case of Frazer and Haggard in which caseating tuberculous mesenteric lymph nodes were observed in the resected specimen though the ileitis proper was nonspecific in origin.

Endarteritis obliterans and perivascular infiltration with collections of plasma cells were emphasized by Binney. Early involvement of nerve tissue particularly Auerbach's plexus was noted by Barbour and Stokes though these changes are not specific. They even suggested that a chronic recurring intussusception might initiate the process by impairing the circulation and vitality of the gut wall. Schepers divides the lesion into two components: a primary phase characterized by (a) a stage of edema of the submucosa and the serosa with dilatation of submucosal lymphatics and hyperemia of juxtamuscular adventitial blood vessels (b) plasma cell infiltration of submucosa and serosa (c) diffuse fibrosis with disappearance of plasma cells (d) healing; a secondary phase characterized by ulceration of the mucosa and submucosa which is superimposed on the primary phase with eventual tendencies to late or early perforation, fistulation and granuloma formation.



FIG 10 Cross section of chronic terminal ileitis showing stenosis of the lumen caused by extensive granular infiltration of the submucosa

There are two more recent thought provoking observations on the pathology of ileitis. In resected specimens Brunner like glands have been observed in the mucosa and in the submucosa in cases of ileitis. These glands are similar to those appearing in the normal histology of the duodenum and the pylorus. Sixteen of 34 such resected specimens show on microscopic study such Brunner like glands most of these cases were later shown to be followed by recurrent disease (Kawel and Tesluk).

Davis Dockerty and Mayo made comparative studies of the number of ganglion cells in the myenteric plexuses of the normal bowel as compared to those of regional ileitis. Persons suffering from regional enteritis possess in the mesenteric plexuses of the small intestine approximately three times as many ganglion cells as person not so afflicted. Regional enteritis of long duration is attended by a greater increase in ganglion cell count than diseases of short duration.

In both these observations the changes observed may be secondary rather than primary in nature as a causative agent in the disease.

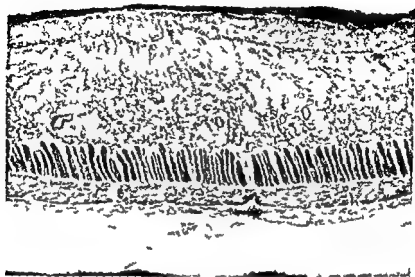


FIG. 9 Longitudinal section of skip lesion. Marked submucosal thickening due to granulomatous infiltration. Epithelium completely ulcerated and surface covered with a purulent exudate.

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next largest group falls between 5 and 20 years before recognition of the disease. The one with a 50 year unrecognized diagnosis was a Hindu from British India. Blackburn states that the average duration of symptoms before operation was $31\frac{1}{2}$ months. Clark and Dixon found that the average duration of symptoms before observation was 4.1 years, the longest duration of symptoms 25 years.

If one were to speak of prodroma one could mention only the suppurative rectal complications which so often precede by years the onset of manifest symptoms. The rectal or perirectal abscesses and fistulas occurred in 86 of 542 cases; the real significance lies in the fact that they so often precede the onset of diarrhea. If they do not actually antedate the diarrhea they are so obvious and the diarrhea so minimal that in most uninitiated observers only the fistula or perirectal abscess exists. On one occasion a patient who was admitted to the ward for routine hemorrhoidectomy was observed to have a small rectal fistula. A resident physician detected a vague history of diarrhea and asked for radiographic study which disclosed a terminal ileitis.

The one other phenomenon that stigmatizes the onset of ileitis is the scar of a previous appendectomy. This scar was evident in 116 or 21.4 per cent of our series of cases and was a signal of previous abdominal pain localized in the lower right quadrant of the abdomen. Ravdin and Johnston in a review of cases published in the literature found that a previous appendectomy had been performed in 27.1 per cent of the cases. The diarrhea which characterizes most of the cases of ileitis was undoubtedly overlooked; the abdomen was opened, an innocent appendix removed, and the ileitis not observed.

The onset of the true symptoms of ileitis or enteritis is characterized when typical by the initiation of diarrhea, abdominal pain, low grade fever, progressive anemia and loss of weight and eventually by the ability of the clinician to feel an intra-abdominal mass. Diarrhea was present in 491 of the 542 cases of regional ileitis. The diarrhea is an outstanding feature of the disease though in number of movements and in intensity it rarely approaches that of ulcerative colitis. The rule that frequency of fecal movements in an inflammatory intestinal process is in inverse proportion to the distance from the anal sphincter holds good. Ulcerative proctitis gives usually 10 to 20 stools a day with urgency, tenesmus and the appearance of fresh blood in the stool. Ulcerative colitis in the distal colon may average 5-10 stools a day; right-sided or segmental colitis is notable for lessened frequency of defecation.

Chapter 4 Clinical Features

Onset

THE USUAL CASE of regional ileitis does not begin as an acute and sudden manifestation its onset is usually hidden in the deep past with such intervening symptoms as an occasional spell of diarrhea a progressive malaise or nervousness often verging on true psychoneurosis A rectal suppurative complication may long precede the manifest initiations of diarrhea Gradually the diarrhea increases in severity and is now accompanied by abdominal pain low grade fever is occasionally noted with loss of weight In the prodromal stages the patient loses little efficiency or time from his work or occupation The progressive symptoms build up over the course of years to the finally fully developed picture of regional ileitis Such is the most common picture of the onset Some unusual forms of onset have been noted in this series e.g. initial intestinal obstruction 4 cases onset with hematemesis and melaena 2 cases onset with dysuria one case onset with sealed off perforation one case

The duration of symptoms before the actual recognition and diagnosis of the disease in this series may be seen in table 6

TABLE 6
DURATION OF SYMPTOMS BEFORE RECOGNITION OF REGIONAL ILEITIS

<i>Duration</i>	<i>% of Cases</i>
0-6 months	0
6-12	37
1-2 year	86
3	78
3-5	86
5-10	96
10-15	47
15-20	34
20-30	15
30-40	1
40-50	

Total 482

It will be seen that the largest group of cases falls between one and 5 years duration of symptoms before the initiation of therapy the

of the ileum that segment which radiographically corresponds to the string-sign. The attempt of the intestinal fluid column to pass through this congested edematous and narrowed stretch of intestinal lumen gives rise to the colicky sensation of pain. The absence of pain occurs in those cases in which the inflammatory lesion is diffuse the mucosal type in which the beginning cicatricial process is still young the mucosal pattern is altered by the stenosing string-sign the quill like narrowing has not yet supervened. The higher the process in the ileum the less likely the stenosis and hence the less likely predefecatory pain. In the late long standing case where true stenosis supervenes the pain is of course severe and sharply colicky. Occasionally primary intestinal obstruction characterizes the onset of regional ileitis or at least its symptomatic phase.

Nausea and vomiting are rare manifestations and occur only in the later stenotic phase of the disease. Appetite is usually well preserved in contrast to ulcerative colitis where loss of appetite absolute anorexia and even vomiting are common manifestations and parallel the intensity of the toxic process. Ulcerative colitis is a much more toxic disease than regional ileitis and the interference with appetite and with nourishment is in contrast to the milder manifestations and retained desire for food which is present in ileitis.

Fever occurred in roughly one third of the cases in this series. The fever is of the low grade type the temperature usually normal in the morning rises to 100.5 degrees 101 degrees or rarely 102 degrees F in the late afternoon. It is irregular in type though often persisting it is not accompanied by chills or sweats. Many if not most of the cases are afebrile throughout. The fever characterizes the acute or inflammatory phases of the process the intervening stages of remission are afebrile the late cicatrizing phase of the disease is also afebrile.

The continuous low grade fever of ileitis like that of segmental or right sided colitis is frequently mistaken where the diarrhea is minimal and unnoticed for many of the other diseases which are also characterized by low grade fever and low leukocyte counts in the circulating blood. In 11 cases in this series the onset of the disease was characterized by fever of unknown origin as the first and presenting symptom. Undulant fever brucellosis subacute bacterial endocarditis and lupus erythematosus disseminatus are frequently the connotations given to the low grade febrile type of ileitis without any noticeable diarrhea or abdominal pain.

perhaps 3.6 per day. Regional ileitis with all its pathologic process proximal to the ileo-cecal valve is noted for mild diarrhea 2 to 4 or 5 movements in 24 hours.

Each individual movement is usually preceded by a spasm of abdominal pain. The characteristic sequence of events is similar to Moynihan's classic description regarding duodenal ulcer—pain food relief pain. In ileitis the sequence is abdominal pain or colic desire to defecate the feeling of sudden rumbling of gas followed by defecation with relief of all subjective abdominal symptoms—so called pre-defecation pain. This sequence may repeat itself every few hours of the day less at night. It is often initiated by the taking of a meal. The defecations are not urgent or spurting in nature. The stool is mushy semi-formed or liquid. It contains some excess of fluid mucus but never evident pus and only rarely blood. In fact occult bleeding in the stool on examination with guaiac is usually negative. The stool may be slightly acid or alkaline or it may be neutral. The reaction here has no significance.

Either a normal number of daily movements or constipation (49 cases) mark the remainder of this series. Not infrequently even in a mature case of ileitis no history of diarrhea is obtainable and in some few cases actual constipation was noted. The presence of constipation does not necessarily denote obstruction since only in the late phases of intestinal obstruction is the constipation acute and obdurate. In those cases in which constipation has been present the remaining symptoms of abdominal pain, colic, a mass and a progressive course have also been negligible. The radiographic study establishes the diagnosis.

Abdominal pain was noted in practically all instances in this series. This fact is not surprising for pain in the abdomen seems so constant a complaint in the anamnesis that one would expect its presence in almost all of the cases. The pain is usually mildly colicky in nature most often situated in the lower abdomen preferring the right lower quadrant or the suprapubic region as its site. Occasionally the pain is solely in the left lower quadrant and in a few cases covers the whole lower and upper abdominal segments. The pain precedes and is relieved by defecation. When the inflammatory mass becomes adherent to the sigmoid loop of colon and pinned down to that viscus by internal fistulas the pain and the mass are likely to be localized in the left lower rather than the right lower quadrant of the abdomen.

The origin of the pain is in the mildly obstructive narrowed loop

of the ileum that segment which radiographically corresponds to the string sign. The attempt of the intestinal fluid column to pass through this congested edematous and narrowed stretch of intestinal lumen gives rise to the colicky sensation of pain. The absence of pain occurs in those cases in which the inflammatory lesion is diffuse the mucosal type in which the beginning cicatricial process is still young the mucosal pattern is altered by the stenosing string sign the quill like narrowing has not yet supervened. The higher the process in the ileum the less likely the stenosis and hence the less likely predefecatory pain. In the late long standing cases where true stenosis supervenes the pain is of course severe and sharply colicky. Occasionally primary intestinal obstruction characterizes the onset of regional ileitis or at least its symptomatic phase.

Nausea and vomiting are rare manifestations and occur only in the later stenotic phase of the disease. Appetite is usually well preserved in contrast to ulcerative colitis where loss of appetite absolute anorexia and even vomiting are common manifestations and parallel the intensity of the toxic process. Ulcerative colitis is a much more toxic disease than regional ileitis and the interference with appetite and with nourishment is in contrast to the milder manifestations and retained desire for food which is present in ileitis.

Fever occurred in roughly one third of the cases in this series. The fever is of the low grade type the temperature usually normal in the morning rises to 100.5 degrees 101 degrees or rarely 102 degrees F in the late afternoon. It is irregular in type though often persisting it is not accompanied by chills or sweats. Many if not most of the cases are afebrile throughout. The fever characterizes the acute or inflammatory phases of the process the intervening stages of remission are afebrile the late cicatrizing phase of the disease is also afebrile.

The continuous low grade fever of ileitis like that of segmental or right sided colitis is frequently mistaken where the diarrhea is minimal and unnoticed for many of the other diseases which are also characterized by low grade fever and low leukocyte counts in the circulating blood. In 11 cases in this series the onset of the disease was characterized by fever of unknown origin as the first and presenting symptom. Undulant fever brucellosis subacute bacterial endocarditis and lupus erythematosus disseminatus are frequently the connotations given in the low grade febrile type of ileitis without any noticeable diarrhea or abdominal pain.

The leukocyte count in the circulating blood in ileitis is not usually materially elevated. The range may be between 9 000 and 12 000 white blood cells rarely higher. A shift to the left of the polymorphonuclear leukocytes and toxic granulations is rarely seen in contrast to severe ulcerative colitis where both these conditions are frequent. Eosinophilia as in ulcerative colitis is common the rate rising to 4 to 8 to 12 per cent in a small number of cases. The explanation of the eosinophilia in both conditions is not apparent. The attempt to explain the eosinophilia on an allergic basis is not satisfactory nor are foreign body inclusions a reasonable answer. The eosinophilia is part of the general systemic reaction to the disease. In acute ileitis the total white count is higher and a greater percentage of polymorphonuclear leukocytes is present in the circulating blood a fact that only intensifies the confusion in differentiating acute ileitis from acute appendicitis. An increased sedimentation rate of the red blood cells is usually observed according to Snapper, Pompen and Groen.

A moderate often progressive anemia characterizes regional ileitis. In advancing cases the hemoglobin reading may range from between 60 per cent and 70 per cent on the Sahli scale lower readings are not unusual even in the absence of gross intestinal hemorrhage. In one case in this series the hemoglobin fell to 32 per cent Sahli without evidence of melaena. In another case twice operated on for recurrent ileitis the severe anemia of 16 per cent hemoglobin was explained when the true picture of a primary pernicious anemia became apparent in the blood smears. An achylia gastrica was present reticulocyte response to liver extract absent in this individual. The pernicious anemia in this case was incidental and probably not related to the regional and recurrent ileitis.

Gastric secretory change in ileitis are unusual. One regularly notes a normal type of curve in the fractional test meal; the secretory curve may however be low (hyporacidity). Apart from the above cited case complicated by pernicious anemia only once was true achylia gastrica seen in this series.

The general symptoms of ileitis are those of weakness loss of strength and loss of weight. A material weight loss was noted in 143 cases in this series in one instance the loss amounted to 50 pounds. In the advanced cases those with intestinal obstruction and following debilitating operation the loss of flesh may be much greater and more extreme in terminal case amounting to emaciation. This extreme

however unusual. The average case may lose 10, 15 or 20 pounds; the patient finds it difficult to regain weight because of the persistent diarrhea and abdominal pain. Following successful operative procedure the regain of weight is rapid and ample. The loss of strength is not extreme; many patients with mild ileitis are able to continue at their work with little loss of efficiency. In one instance a man in the Armed Forces during the Second World War was able to continue in active service for 3 years after the onset of diarrhea, which signalized the initiation of the ileitis, the diagnosis then being unrecognizable or unrecognized. In a man 71 years of age who complained of anorexia, weakness, moderate diarrhea and a loss of 25 pounds of weight, simulating cachexia, the entire clinical picture was one of marked carcinomatosis. Repeated x-ray examinations of the gastrointestinal tract were reported as negative. Eventually, exploratory operation revealed a regional ileitis involving 60 cm. (24 inches) of terminal ileum.

Retarded growth and delayed secondary sexual maturation in children was occasionally noted in this series of regional ileitis. Where the higher reaches of the ileum and the jejunum are involved, the interference with growth and maturity will be observed to be much higher.

Menstruation is usually regular and maintained in contrast to ulcerative colitis, where amenorrhea characterized the more severely toxic nature of that disease.

Joint pains were present in 17 cases in this series; the larger joints, such as ankle, knee and elbow, being usually involved, as is so commonly seen in segmental colitis. The small joints of the hands and feet are spared in ileitis. Clubbing of the fingers of the hand occurred 22 times in this series. Erythema nodosum was observed 7 times, usually, but not always, associated with arthritis.

The nervous or rather psychic manifestations of this disease are sometimes so manifest that they overwhelm the true somatic manifestations. This occurred in 18 cases in this series that we know of, probably much more often. In 6 of the cases the onset of symptoms occurred while the patients were in active service in the Armed Forces. Most of the cases were regarded as psychoneurotic following exposure to battle or due to bomb shock; some were classed as nervous diarrhea or as food poisoning. In civilian life 10 cases were treated as depressions or as neurasthenia. 8 of them in institutions for mental care. The evident psychic and nervous symptoms that accompany ileitis often lead to

delayed recognition of the true causes for the symptoms. Of Blackburn's 22 cases one suffered from a true psychosis and 4 were referred to psychiatrists for mental treatment when as he states a routine clinical pathological and radiological investigation would undoubtedly have shown organic disease of the ileum.

However ileitis can hardly be classed as a psychosomatic disease. Occurrences or recurrences do not follow upon psychic shock as evidently as they can be observed in ulcerative colitis with relationship of cause to effect.

Physical Examination

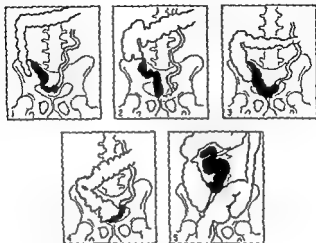
The two outstanding features in the physical examination of the cases of regional ileitis are (1) an abdominal mass and (2) evidence of fistula formation external and internal.

The abdominal mass (observed in 185 cases in this series) is usually found in the right lower quadrant of the abdomen in an anatomic area corresponding to the inner surface of the cecum. The mass varies in size from that of a finger to that of a lemon, a large orange or occasionally even larger. The mass is usually fixed to the posterior wall to the cecum or to the anterior abdominal wall particularly when an external fistula is present leading anteriorly from the mass. Tenderness on palpation is constantly present when the mass is small and in its typical site it is with difficulty differentiated from a spastic cecum. The mass consists materially of the inflamed terminal loop of ileum and of adherent loop of nearby ileum or of cecum, ascending colon or sigmoid.

When the segments of the mass are separated at the operating table it will usually be seen that the intestinal loops are adherent because of single or multiple intercommunicating fistulous tracts. The mass particularly when adherent to the dome of the urinary bladder may be apparent in the lower midabdomen. In one instance simulating a urachus cyst. In another instance the loops of ileum were adherent to and drawn over by the sigmoid colon the mass being palpable to the left of the midline of the abdomen.

The most common seat for the mass is low in the right lower quadrant of the abdomen palpable frequently by rectal or vaginal pelvic examination or by bimanual technique. This fact is easily explainable the position of the terminal ileum is dependent from the cecum. Testut places the cecum below the pelvic inlet in 15 per cent of males and in 30 per cent of female bodies. In the upright position the cecum and loops of

terminal ileum fall into the pouch of Douglas in the female and between the bladder and rectum in the male. Very often these loops lie directly



NORMAL TERMINAL ILEUM
VARIATIONS IN ANATOMICAL POSITIONS

FIG. 11. Anatomic position of the normal terminal ileum.

(1) Usual position of cecum and ileum. (2) High cecum ileum descent to pelvis. (3) Low cecum medial implantation of ileum. (4) Complete descent cecum and ileum in pelvis. (5) Exceptional position ileum in abrupt ascent.

on the pelvic floor (fig. 11) supported by the levator ani muscle. Monks found the terminal ileum to be in the pelvis in more than 50 per cent of his studies. In our own radiographic studies made to determine the position of the normal ileum it was found (Crohn and Yarnis) that in 150 control normal cases descent of the cecum and terminal ileum into the lower pelvis occurred in 28 per cent of the observed cases in that series. In the pathologic ileum (25 cases of terminal ileitis) the terminal affected loop of ileum was found in the pelvis in all cases—in fact on the floor of the pelvic cavity (fig. 12). It is apparent that the soggy, weighted diseased ileum descends low down in the right lower abdominal quadrant and being even heavier than normal in weight occupies almost uniformly the pelvic inlet. The mass of ileitis is then found and easily palpated by bimanual technique in the fossa of Douglas. Only when adherence to other organ takes place is the mass felt other than in the right

delayed recognition of the true causes for the symptoms. Of Blackburn's 22 cases one suffered from a true psychosis and 4 were referred to psychiatrists for mental treatment when as he states a routine clinical pathological and radiological investigation would undoubtedly have shown organic disease of the ileum.

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festations indicate the degree of general body affection a part of the localized intestinal process

Erythema nodo um on the anterior aspect of the lower extremities was noted once in acute ileitis and 11 times in chronic regional ileitis This phenomenon which is so much more prevalent in ulcerative colitis possibly links the two diseases in a common etiologic factor

Obstructive Phenomena

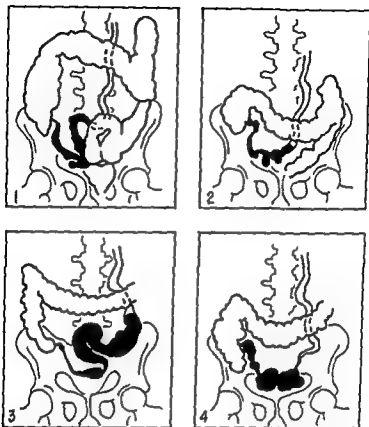
Intestinal obstruction occurred in 45 instances in this series of 542 cases usually late in the course of the disease Four times in the series it was an early—in fact the presenting—symptom at the onset in the other cases it indicated a long standing chronic inflammatory process eventuating in chronic cicatricial stenosis of the bowel at the site of the lesion Sherill and Hall indicate two cases with obstruction as the initial phenomenon though both were old chronic cases Jackman reported two cases of hypertrophic enteritis as a cause of intestinal obstruction—both of the acute type—in which the terminal ileum was perforated during the operative manipulations

Occasionally the obstruction may be due to angulation and kinking of a loop of bowel by peritoneal adherence or by ileo ileal fistulation Loops of distended intestine may be seen through the thin abdominal wall visible peristalsis is not uncommon and is accompanied by severe abdominal cramps and borborygmi A scout film of the abdomen will show puddling and fluid level Vomiting may be present in the more severe stenotic phases The obstruction can usually be temporarily alleviated by the use of the Miller Abbott or Harris tube

Postoperative intestinal obstruction such as characterizes many cases of intestinal resection or short-circuiting operations is unfortunately only too frequent but happily does not occur as frequently as in reconstructive surgery for ulcerative colitis

Pancreatic Insufficiency in Regional Ileitis

It is interesting to note that both in regional ileitis and in ileo jejunitis Dreiling found evidence of pancreatic insufficiency in a fair percentage of such cases By means of the secretion test he demonstrated low maximum HCO_3 concentrations in three instances and low total amylase estimation in 5 out of 22 subjects submitted to the test A moderate degree of pathologic change namely fibrosis has also been reported



VARIATIONS IN ANATOMICAL POSITIONS OF ILEUM IN TERMINAL ILEITIS

FIG. 1. Anatomic position of diseased ileum. The weight of the diseased ileum carried it downward to lie in the pelvic floor.

lower abdominal cavity. When fistulous tract burrow into and through the appended base of the mesentery, the necrotic process may cause a diffuse suppurative mesenteritis which participates in and increases the size of the inflammatory mass.

Apart from the abdominal mass and the demonstration of characteristic fistulae, the physical examination of the cases of ileitis is likely to be negative. Enlargement of the spleen was noted 6 times; clubbing of the fingers 22 times—not necessarily in the same patient. Both mani-

in 2 instance just knocking the diseased bowel wall accidentally during operation resulted in immediate fistula formation in the healing incision even though great surgical care was immediately exercised in suturing the cut in the wall of the ileum

Spontaneous fistulas to the abdominal wall without a previous laparotomy have not been observed. But unusual exit sites for external fistulas are occasionally noted. Multiple external fistulas to the inguinal region have been noted twice at least 4 fistulas in one instance there being no previous operative scar. Hurst has noted a fistulous tract originating in the ileum and pointing downward and infiltrating the extra peritoneal tissues in the right groin. Brown and Donald reported 47 cases with fistula formation out of a total of 178 cases an incidence of 26.5 per cent. This is a higher incidence of fistulation than that encountered in this present series or in most of the current literature. They further state that fistula formation occurs invariably only after surgical procedures.

Ileo psoas fistulas to the lumbar region have been seen 3 times twice by the author and once mentioned and reported by Snapper where

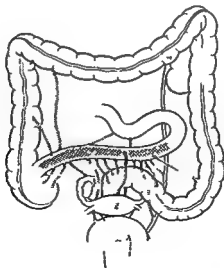


FIG. 13 Multiple fistula ileum to adjoining hollow viscera. Note termination in unusual sites a right fallopian tube b left ureter body of uterus

Chapter 5 Fistula Formation In Regional Ileitis

FISTULA FORMATION is the most constant clinical and pathologic phenomenon in ileitis. These intestinal fistulas are of three types: (1) fistulas to the anterior abdominal wall; (2) internal fistulas between loops of bowel and adherent hollow viscera; (3) rectal and perirectal fistulas.

Fistulas to the anterior abdominal wall are among the most common types of fistulation and occur exclusively in the site of the scar of a previous laparotomy. The antecedent operation in most cases (30.6 per cent) was an appendectomy. We encountered 47 instances of anterior wall fistulas, all of them in the appendectomy scar or in the scar of a previous exploratory laparotomy. Fistulas to the abdominal wall are infrequent after simple appendectomy for acute appendicitis (Ginzburg). According to Colp, in 2840 cases of acute appendicitis abdominal wall fistulas were found only 33 times, an incidence of 1.1 per cent, only 3 required reoperation. Clark and Dixon, in 44 cases of regional enteritis, found 9 external fecal fistulas, one of which passed feces and gas through the urethra. Four of these 9 patients also had intractable fistulas, one a fistula in the urinary bladder.

In some of the instances of ileitis, not single but multiple fistulas were present. In one case, 4 anterior wall fistulas in several scars of 8 previous laparotomies (Crohn).¹ These fistulas occur usually within a few weeks of the apparent healing of the operative scar. The scar becomes reddened and inflamed at a localized area, a low grade fever becomes apparent with regional pain and tenderness. An abscess forms and either breaks spontaneously or is incised, following which fecal drainage occurs and a chronic fecal fistula is established. In some instances the abdominal wall fistula occurs only months or years later, 2 years, 4 years, and in one instance 8 years after a presumably successful resection for terminal ileitis. The 8 intervening years were marked by excellent health until the appearance of the fistula signaled a recurrence of the ileitis.

These external wall fistulas are apparently very facile of creation.

segment of the large bowel or in any adjoining hollow intra abdominal viscus such as ureter urinary bladder uterus or fallopian tube

The internal fistulas were noted in 95 of our cases (approximately 17.5 per cent) though the incidence of such internal fistulas would appear in practice to be much higher. Variations of the internal fistulas are listed in table 7

TABLE 7
VARIATIONS OF INTERNAL FISTULAS

<i>Site of fistula</i>	<i>No. of Cases</i>
Ileo-cecal	39
Ileo ileal	18
Ileo sigmoid	18
Ileo vaginal	4
Ileopsoas	
Ileovaginal	1
Urinary (Ileum to urinary bladder)	1
Ileum to uterus	1
Total	95

On two occasions the opening of the fistula into the sigmoid colon was seen by sigmoidoscopy. In two other instances the fistula which broke into the right fallopian tube gave rise to a salpingitis discovered inadvertently by a gynecologist operating for supposed adnexal inflammation. The discharge of the proteolytic content of the fistulous tract into any hollow viscus usually terminates its course.

Probably the most common of all the internal fistulas are those of the ileo-ileal variety; they are readily demonstrated at the operating table (figs 14-15). Many or most of these fistulous tracts are notable and visible in the preoperative radiographic films provided that their presence is diligently searched for. The fine lines seen with a magnifying lens emanating from the diseased ileum indicate potential fistulas (fig 15). These are frequently seen overlying the dome of the urinary bladder and creating urinary symptoms. Actual gross fistula exit into the urinary bladder is rare in ileitis much less common than are such similar fecal fistulas which arise in a sigmoid diverticulitis. Forbes and Duncan report an interesting case of ileitis in which a large fistula existed between the terminal ileum and the urinary bladder; the patient passed gas and fecal material through the urethra. Ileo-transverse colostomy without transection of the ileum was performed but the intestinal symptoms and those of the ileovesical fistula persisted. At a second operation

a series of external fistulas occupying the right lumbar area were observed expelling vegetable matter and fecal content. The fistulas were traced to a terminal ileitis. The linear extent of these intestinal fistulas gives rise to some speculation as to their nature. They are apparently lytic rather than infectious in type. They traverse large areas of mesentery and distal fascial planes without giving rise to infection, terminating their course by finding an exit point somewhere on the surface of the body. They are lytic or proteolytic, the activated intestinal or pancreatic enzymes of the fecal chyme slowly digesting their way through planes of fascia and muscle to exit on the body wall. Such fistulas become infected and suppurate only as a result of skin bacterial contamination at the point of exit from the abdominal cavity.

Internal Fistulas

The mechanism of formation of internal intestinal fistulas is identical to that of external abdominal wall fistula. These tracts originate in the sodden, porous, ulcerated terminal ileum, usually on the side of the mesenteric attachment. They traverse the mesentery of the small bowel and terminate in an adjacent loop of small intestine in any

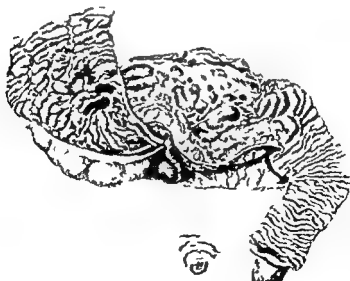


FIG. 14. Combined ileocolitis. No fistulous tract between ileum and base of cecum. Meckel diverticulum not involved.

Perirectal Fistulas

In 1934 Bissell published a case report of terminal ileitis in which multiple rectal fistulas occurred as a complication of the intestinal disease. He felt that the presence of the inflammation of the ileum in the cul-de-sac could easily have given rise to the rectal abscess and persistent rectal fistula. In 1938 the diagnostic significance of perianal, rectal and recto-vaginal fistulas was emphasized²⁰ (Penner and Crohn). In that publication 20 cases of perirectal fistulation were noted in a group of 110 cases of ileitis, an incidence of 18.2 per cent. This was almost equal to the combined number of external abdominal wall fistula (12 cases) and internal intestinal fistulas (11 cases) as shown in that series. The total incidence of fistula formation in this series of 542 cases can be summed up as follows:

In the present series of 542 cases of regional ileitis, perirectal abscesses and fistulas were noted 77 times, an incidence of 14.2 per cent; this does not include 9 instances of recto-vaginal fistulation. The total number is somewhat below the combined number of external (47) and internal fistulas in this present series (95), which equals 26.2 per cent. This equals 4.2 per cent of all cases.¹

TABLE 3

<i>Type of Fistula</i>	<i>No. of Cases</i>
External abdominal wall fistula	47
Ileo-psoas	2
Urethral	12
Inguinal	1
Internal intestinal to neighboring viscera	79
Perirectal or recto-vaginal	86
Total	227

Jackman and Smith in 1943 recorded 36 cases at the Mayo Clinic of anal abscess or fistula in a group of 114 cases (31.6 per cent), a figure high above those in this series. They included those cases that had a history of operation for anal fistula within a 3 year period prior to their initial visit. Eight of the series of 114 cases came to the Clinic primarily because of anal fistula, the intestinal disturbance being so mild as to have been overlooked.



FIG 15 Terminal ileitis. Fistula ileum to sigmoid

the ileum distal to the anastomosis was transected as the sole procedure except for a temporary ileostomy of the distal ileal loop. Within four months the patient gained 25 pounds in weight and was free of symptoms while the dysuria and passage of gas and feces per urethra had disappeared. Unfortunately, a severe recurrence of the ileitis took place after the date of publication of their article. In another case cited by these authors, an ileovesical fistula persisted for some time in spite of an ileocolostomy. This fistulous tract was resected and broke down again with the secondary formation of an additional fecal fistula, but eventually both fistulous tracts healed with subsidence of all symptoms.

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TABLE 2

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Perirectal or recto-vaginal	18
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FIG 16 Perianal fistulas in regional ileitis

Method of Anal Fistulation

Either of two methods may explain anal suppuration

1 Most of the fistulas occur as a result of infection in the rectal crypts of Morgagni above the anal sphincter the contaminated fecal infectious material being transported thereto by the propulsion of the fecal column. The infection of the crypts gives rise to a perirectal abscess or an ischio rectal abscess which opening simultaneously on the surface of the buttock and within the anal canal forms a permanent fistula. When the abscess localizes anteriorly in the female it may break simultaneously through the perineal body into the vagina and posteriorly into the rectum forming a recto vaginal fistula.

This type of local rectal infection in ileitis is almost identical to that seen in ulcerative colitis. In both the internal opening of the fistulous tract is just within the anal margin in the recto vaginal fistulas the anterior opening is just within and above the fourchette constituting a small opening which emits a thin fecal leakage.

2 The second method of fistulation to and about the anus and perineum is more problematic. This fistulas tract is considerably more circuitous proteolytic material escapes from the porous terminal loop

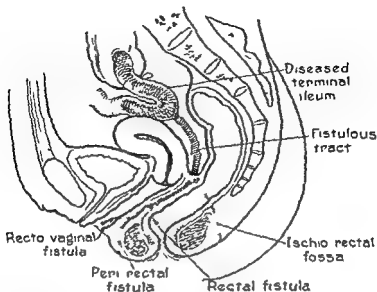


FIG. 17 Gravity fistula—route of direct fistulation terminal ileum to perirectal space

of ileum lying heavily on the pelvic floor. The material seeps downward through the pelvic peritoneal reflection and the retroperitoneal fat and burrows through the pelvic fascia following the planes of the levator ani muscle (fig. 17). The material makes its exit into the rectum above the sphincters or piercing the slinglike attachments of the fibers of the levator ani and makes its exit at the perianal margins. The ischio-rectal fossa may be contaminated forming an abscess which will reveal itself as a perirectal fistula communicating internally with the rectum. Attempts to follow such long fistulous tracts are difficult; lipiodol injected into the tract from below will ascend for several inches but will be lost somewhere in the pelvis; a streak of barium following a radiographic study may be seen pointing downward in the same direction. A direct and continuous path has not been unequivocally demonstrated except in one case in the literature where at autopsy the continuity of the path was clearly dissected (Patricelli).

The diagnostic significance of perianal fistulas has not been sufficiently appreciated. They may occur one to 14 years before the onset of active diarrhea and abdominal pain constituting the early prodromal manifestations of the disease.

It is a fair statement to make as a generalization that suppurative perianal fistulas in the presence of diarrhea indicate a pathologic inflammatory process somewhere in the intestinal tract. These fistulas occur with great frequency in ileitis, ulcerative colitis and intestinal tuberculosis. They do not occur in nervous, gastrogenous, pancreatic, allergic or thyrogenic diarrhea. Exceptions to this general rule have been very rarely noted.

Chapter 6 The Course in Regional Ileitis

REGIONAL ILEITIS may begin as an acute phase of the disease or it may be first observed as an acute exacerbation of a pathologic process which has been overlooked. In the vast majority of cases it comes under observation as a disease of great chronicity. The acute case simulating acute appendicitis (except for the presence of diarrhea as a symptom) resolves in 66 per cent of the cases without further evidence of recrudescence. The remainder of the acute cases subside spontaneously, usually in spite of the laparotomy and customary appendectomy, and lapse into the low grade typical chronic course of the disease.

The course of long standing chronic regional ileitis is one of great chronicity. Spontaneous remissions that endure for year may occur during which remissions the diarrhea will abate or be absent, the temperature remain normal, appetite be preserved and nutrition be only slightly impaired. Except for a slight and slowly progressive loss of weight, mild persistent anemia and occasional short bouts of diarrhea and abdominal pain, the patient may follow a normal career of physical well being and school or occupational activity. If the disease intensifies in the intestinal tract, the period of activity will be greater and will last longer, the remissions become shorter. In time either the continuous diarrhea or the loss of weight and strength will indicate the progression into a most severe phase of the disease. Eventually the onset of obstruction (45 cases) will supervene with abdominal pains, vomiting and the ability to feel an abdominal mass on palpating the abdomen. At any time in the course of the disease a perirectal abscess or a fistula in the scar of the abdominal wall may supervene.

In the continued study of chronic regional ileitis with the assistance of radiographic observation it will be noted that three variations in the course must be considered. In the first group spontaneous healing of the lesion with disappearance of all radiographic evidence will supervene. This occurred in 5 of the series of 542 cases of regional ileitis. The second group is constituted of cases in which anatomically the lesion remains static, usually localized to the terminal ileum, progression up-

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have however been observed radiographically to show the lesions remaining stationary. This applies even in cases where skip lesions are already demonstrable.



FIG. 18. Terminal ileitis; conservative medical therapy. At onset—volume of 12 inches of ileum.

CASE D.V. A 34-year-old woman with regional ileitis. The volume of the ileum was demonstrated radiographically as follows:

January	24 1953	dilat 12-14 inch
June	9 1953	12-14
November	15 1954	12-14

ward of the pathologic process cannot be radiographically demonstrated. In the third group the lesion is obviously a progressive one and continues to spread mildly either continuously or by skip lesions until the upper reaches of the ileum or the jejunum become involved.

Group 1 (5 cases)

Chronic Long standing Regional Ileitis with Spontaneous Healing

It was surprising to note that spontaneous healing with roentgenographic proof could take place in regional ileitis even in cases where internal fistulation had been radiographically demonstrated. In these 5 cases the diagnosis had been first observed and confirmed at the time of previous appendectomy. For example:

1. A woman 32 years of age with a fistula to the abdominal wall, a tubo-ovarian abscess and a palpable mass. Radiographically 2-3 feet of ileum were involved. She was well after 4 years.
2. A man 45 years of age, the whole ileum was involved. He was well 3 years later.
3. An 18 year old girl with involvement of the mid ileum and jejunum with clubbing of the fingers. Three years later under corticosteroid therapy she was well and a radiographic study of the small bowel was negative.
4. A 20 year old female with involvement of 10 inches of mid ileum. She was well and the radiographic study was negative 3 years later.

It will thus be observed that in a minority of fortunate individuals an apparent spontaneous cure is possible; fistulas internal and external under exceptionally favorable conditions are capable of self-healing. Restoration to normal health and well-being seems possible.

These observations on self-healing are made with the reservation that relapses have been noted even after as long as 9 to 27 years of apparent health and in spite of apparent surgical cures. The final word on the life history of the disease as pertains to self-healing may require future elaboration.

Group 2

Chronic Regional Ileitis without Progression (figs. 18-20)

The exact percentage of cases in this group cannot be stated since comparative radiographic studies over the course of years is not often capable of fulfillment (figs. 21 and 22). A sufficient number of cases

have however been observed radiographically to show the lesions remaining stationary. This applies even in cases where skip lesions are already demonstrable.



FIG 18 Terminal ileitis—conservative medical therapy. At onset—involve-
ment of 12 inches of ileum.

Case D.A. A 34-year-old woman with regional ileitis. The involvement
of the ileum was demonstrated radiographically on

January 24 1953	d tal 12 14 inches
June 9 1953	12 14
November 15 1954	12 14

Case D R An 11 year old girl with the following radiographic studies

November 26	1948	Terminal ileum negative
September 25	1950	Questionable involvement of terminal ileum
December 8	1950	Terminal 6 inches involved
March 16	1951	
October 3	1956	" "

There was some evidence of healing the lesion was regarded as minimal in extent and depth

Case E H A 35 year old woman whose x ray studies were as follows

October 15	1955	Two loops of distal ileum involved
November 11	1955	
July 31	1956	
February 4	1957	



FIG 19 5 en m nth aft r onset

These are typical example demonstrating the fact that the disease chronic and granulomatous in nature will remain without progression upward for long period of time if not indefinitely

These cases without extension of the disease over the course of



FIG 20 One year and two month after medical treatment. Note no progression of lesion anatomically.

years seem to lend themselves best to surgical intervention. While late intestinal obstructions, often characteristic of this chronic type, recurrences after operation are less likely to occur. This group should be the most satisfactory for surgical care. In one case the lesion was recognized at exploratory operation 18 years ago; the true nature was not recognized and no further surgical intervention was attempted. The disease lay dormant and presumably asymptomatic. Recurrence of diarrhea and a positive x-ray picture led to operation and resection of the persistent and unextended lesion in the terminal ileum.



FIG. 21 J. G. Regional ileitis 1951

Group 3

Chronic Regional Ileitis with Progressive Extension (Mucosal Type)

The cases are the cases in which the study of the life history of the disease over a course of years reveals active progression of the lesion in an oral direction. Again there are insufficient personal observations to allow any percentages to be offered but an occasional observed case is illuminating.

Case 1 M.H. Male aged 42. In 1935 exploratory operation for terminal ileitis, fistula in ano. Fight to 10 inches then involved no resection. In 1943 8 years later whole ileum involved up to jejunum. Hypoproteinemia marked emaciation.



FIG. 2 J. G. Same case 1957

CASE 2 (figs 23-26) M.H. Female married 51 years of age First seen June 1947 For the last 13 months suffered with mild diarrhea and attacks of bloating and of abdominal cramp. She had been constantly uncomfortable after eating. She had gained a loss of 30 pounds in weight in the last 6 months. The date and the result of the various radiographic examinations were as follows:

October	1946	8-10 inches of terminal ileum involved
March	1947	10-1
June	1947	18
December	1947	60

In this last case in which the successive radiographs were present for comparison the oral progress of the lesion was capable of clear demonstration (figs 23-26)

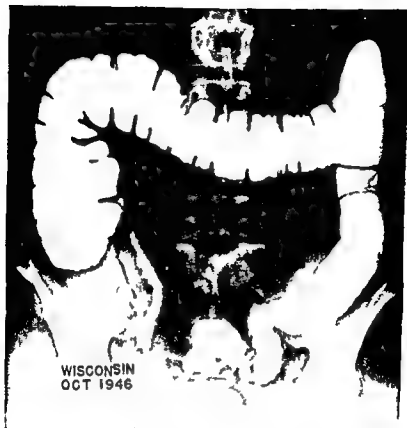


FIG. 3 Octobre 1946—terminal ileum

FIG. 23 26 Mucosal or submucosal type of progressive ileitis. Observations extend for little more than a year.

In this present series there are only 7 instances of rapid progression of the disease the so called mucosal type. One case after a 7 year follow up was well. 5 of the cases continued to be severely ill, one case died. All in all one gains the impression that the rapidly spreading mucosal type of the disease presents a poor prognosis.

It is likely that it is the so called mucosal or submucosal type of case that gives the disappointing results after surgical therapy. The rapid progression probably indicates that much more of the upper bowel is involved than is demonstrable on the x ray films.

In the chronic case of regional ileitis remission of long periods may be observed. Such periods between recurrences of diarrhea and fever



FIG 24 April 1947—two terminal loops involved



FIG 25 June 1947—whole ileum involved



FIG. 26 November 1947—whole ileum and lower jejunum

have been noted to cover up to 5 and 10 years. In one case the onset of symptoms dated 8 years after a previous appendectomy due supposedly to chronic appendicitis. In the later stages of the disease the symptoms become increasingly severe, the recurrences more frequent and of longer duration until continuity of severe complaints causes complete disability.

Chapter 7 Complications of Regional Ileitis

Perforation of Intestine

ACUTE FRANK PERFORATION with generalized peritonitis is extremely rare but can occur. Slow walled off perforation is manifest particularly in the acute instances. 8 cases in this series. In the chronic cases it is not uncommon for laparotomy to reveal a walled off abscess about the inner surface of the terminal ileum limited by the neighboring loops of ileum and the mesal wall of the cecum the whole being agglomerated in one confused mass. When the loops of involved ileum are separated there may be a gush of a small quantity of pus. The neighboring loops are covered with a fibrinous shaggy peritoneal deposit. A small quantity of inflammatory cloudy fluid may be present in the peritoneal cavity (300-400 cc.) The granulomatous low grade type of infection with concomitant fibroblastic reaction precludes the occurrence of free open perforation with only rare exceptions. Attempts to resect terminal ileitis in the presence of a walled off abscess with localized peritonitis is fraught with a high operative mortality. Arnheim report acute perforation of five days standing in a chronic ileitis death occurred before operative interference. Two perforations of the terminal ileum were observed with localized abscess and peritonitis.

Hemorrhages

Gross hemorrhage was noted in 25 instances in this series usually in the course of the disease occasionally (twice) as an initial symptom. The hemorrhage usually occurs in the form of a melaena (23 instances) twice hematemesis was noted once as an initial manifestation of the disease. Fallis quotes a case with repeated profuse and massive hemorrhage passed by the bowel (melaena) two previous x ray examination had been negative. Eight transfusion were required to control shock. Eventually at operation 21 inches of ileum were resected with cure. Galambos and Nittleman cite a case of atypical terminal ileitis in which gastric hemorrhage and melaena dominated the clinical picture and led to the presumptive diagnosis of a peptic ulcer. Yumich and Crohn reported

the case of a 55 year old male whose onset of symptoms was ushered in by two massive intestinal hemorrhages in the form of melaena producing syncope and collapse. The second hemorrhage was almost fatal.

Since one now accepts the fact that the duodenum and even the stomach can be involved in the inflammatory process we must also look to the upper gastrointestinal tract for a nonspecific cause for hemorrhage. This problem is further complicated by the fact that duodenal ulcer occurred in 18 and gastric ulcer in 2 of our cases. While there is probably no relationship between the incidental finding of peptic ulcer and ileitis gross hemorrhage in the course of ileitis may be complicated by the presence of an existing or preexisting peptic ulcer of the usual variety.

General Complications

Peptic ulcer was noted 20 times, cholelithiasis 3 times and acute cholecystitis was encountered once during an operation for terminal ileitis. Regional enteritis involving a Meckel's diverticulum has been observed (Horn and Rhoads) in one case with perforation at the base of the sac. In our own series we have once seen Meckel's diverticulum involved in a skip lesion. In another case a Meckel diverticulum causing low intestinal obstruction by torsion was clinically preoperatively mistaken for a case of ileitis. Patricelli also mentions a case of regional ileitis with Meckel's diverticulitis with fatal outcome.

Some general complications that occur are actually incidental and not related to the disease. Thus this series includes 4 cases with chronic rheumatic heart disease, one with a decompensated right heart on the basis of generalized arteriosclerosis. In 17 cases in this series arthritis occurred as a complication, the large joints usually being involved, one case involved the cervical spine. In 7 instances erythema nodosum on the lower extremities was also visible. Von Patten observed polyarthritis of the rheumatoid type in 27 (45 per cent) of his series. Infectious mononucleosis occurred in 6 individuals as an intercurrent disease. In an unusual case active pulmonary tuberculosis was present though the rectified ileitis was characteristically of the nonspecific granulomatous type. In this case too diffuse involvement of the large joints was noted. Infantilism and delayed sexual maturity has already been mentioned. One case observed had had a large retroperitoneal or intraabdominal abscess with consequent obstruction of the inferior vena cava.

Tetany in regional ileitis is uncommon occurring more frequently in the cases of diffuse disease involving the upper ileum and jejunum.

One case following two resections of the small bowel for recurrent ileitis developed typical carpopedal spasm. Blood calcium in this case was 6.7 milligrams per cent. Immediate relief was noted upon injection of calcium gluconate and control of the diarrhea. In another case typical tetanic convulsions were noted with a blood calcium of 3.4 milligrams per cent. Renal calculus occurred 7 times in this series.

Amyloidosis does not occur in any of the cases in this series in spite of the long duration and chronicity of the disease. This is probably due to the nonpyogenic nature of the discharge from the surface fistulas or in the intestinal flux.

Primary amyloidosis of the alimentary tract has been reported by Golden in a Negress observed for 16 years who was presenting symptoms were hematemesis, dyspnea and orthopnea. At autopsy the stomach, duodenum and terminal ileum were all involved; the liver, spleen, kidney and adrenal were free of amyloid. This, however, is different from true primary regional ileitis in which the systemic amyloidosis is a sequel or a complication. In primary systemic amyloidosis the gastrointestinal tract may be involved as may any other organ; involvement of the arterioles and of the stroma occurs frequently in the intestine. However, systemic amyloidosis secondary to ileitis or nonspecific ulcerative colitis is extremely rare (Koletsky and Stricker, Moschowitz, Cohen and Fishman).

Gaucher's disease was seen in 1 case of ileitis as an incidental finding. Pernicious anemia was seen in one case in this series in a man 54 years of age who had undergone a short circuiting operation for regional ileitis followed promptly by a recurrence of diarrheal symptoms. At a second operation the original site of the disease, the terminal ileum and the ascending colon were resected but no recurrence of the disease process in the new proximal ileum was noted. An unusually severe anemia and emaciation followed this operation. Two years later the blood count revealed a true primary pernicious anemia: hemoglobin 26 per cent, RBC 1,400,000, WBC 2,650 cells; myelocytes one normoblast, marked anisocytosis and poikilocytosis, hematocrit 10.8 per cent, total proteins 4.6 per cent. Sternal marrow puncture 38 per cent myeloblasts. The administration of liver extract was followed by a dramatic response of reticulocytes to 30 per cent. On discharge the hemoglobin was 60 per cent, total proteins 6.1 grams per cent.

According to Argentinian writers^{9, 2} osteomalacia is not uncommon in all disease characterized by disturbance of fat absorption and

affects mostly the lumbar spine. In 2 cases of regional ileitis the osteoporosis was present in a discreet form in the lumbar vertebrae.

Despite the severe suppurative intra abdominal complications which accompany walled-off perforations in ileitis, pylophlebitis and multiple liver abscesses are rarely seen. The report of Snively is the only one to be found in the literature: a Negro male suffered with diarrhea and high fever; ascites was probably present. On one occasion only cysts of *ameba histolytica* had been found. At examination regional ileitis involving 5 feet of ileum was noted: a fistulous communication between terminal ileum and the sigmoid was present as also were pylophlebitis and multiple small liver abscesses. No such complication of ileitis is seen in this series: probably for the reason that almost all cases are instances of granulomatous rather than of suppurative disease. Warren and Sommers quote an additional case in a Negress in which autopsy disclosed thrombosis of the inferior vena cava and external iliac veins following upon intestinal obstruction and complicated by numerous internal fistulas. They mention also one case of mucous cell carcinoma in regional ileitis. In the present series we too have observed one case of adenocarcinoma in a typical instance of ileo jejunitis: the carcinoma was situated in the mid jejunum. Intussusception is not mentioned in the literature as a complication of ileitis.

Gynecologic Manifestations

There is little disturbance of endocrine function in the female as a result of ileitis. Menstruation is not affected even in the severe cases. This is in contrast to ulcerative colitis in which amenorrhea is a frequent manifestation of the severe and toxic phase of the disease: the return of the menses usually indicate the improved prognosis and the beginning of a remission.

Fertility is unaffected by ileitis: pregnancy having been noted frequently in this series particularly during the remission.

Pregnancy as a Complicatory Factor in Ileitis

It has by now been fairly well established that ulcerative colitis and pregnancy are poor concomitants. Patients with active colitis who become pregnant do badly. Even inactive colitis cases in the presence of gestation may have a stormy course and if they pass the second and third trimester without a recurrence they frequently suffer during the

postpartum period. Colitis arising de novo during the pregnancy or in the postpartum period are likely to be serious cases.

What is the result when an ileitis patient becomes pregnant? Our experience as published in 1956 (Crohn Yarnis and Korelitz) comprises a study of 84 pregnancies in 53 patients who either had had ileitis or had ileitis at the time of fecundity. These cases were divided into four groups for comparative purposes.

Group I Known ileitis whose disease was *inactive* at the time of conception. There were 34 patients who had 45 pregnancies during a quiescent period of the disease. Twenty-eight or 62 per cent had uneventful pregnancies. 7 had a recurrence of the disease during the carrying period. 10 had postpartum recurrences of active symptoms making 38 per cent unfavorable.

Patients who had had prior surgery did better. 81.5 per cent came to term without recurrence of the symptoms of the disease. In this group patients without prior surgery fared poorly, only 27.7 per cent survived the pregnancy without a recurrence of active symptoms. Most of the recurrences took place in the second and third trimesters (6) and an equal number in the early postpartum months. The advantage of prior surgery is quite evident.

Group II Ileitis *active* at inception of pregnancy. This group comprised 23 patients with 30 pregnancies at a time when the ileitis was in an active phase. In 3 instances the ileitis was mild, in 22 it was moderately severe and in 5 it was markedly active at the time of conception.

Of these 30 pregnancies in 14 the disease subsided, in 12 the course of the disease remained unchanged, aggravation of the course of the pathologic process was observable in 4 instances. But of the 14 cases that passed through an uneventful course during gestation, 10 of them had postpartum recurrences. Those without prior surgery fared fairly well. In 26 per cent of the 30 pregnancies in this group the course of the pregnancy was unaffected by the intestinal disease, but 12 of these successfully terminated pregnancies showed postpartum recurrences.

Group III Ileitis *beginning* during pregnancy. This group comprised only 3 cases. In this group there were no full term pregnancies. The only fatality in the entire series took place in this group. Regional ileitis beginning during pregnancy constitutes a serious threat to both fetus and mother.

Group II - Ileitis beginning in the postpartum period. This group comprised 6 cases, the disease appearing usually immediately postpartum or in the first or second months following parturition. Four of these patients soon improved, one required surgical intervention, and 2 have continued with mild recurrences of ileitis. In general, postpartum ileitis follows a relatively mild course.

Broadly, one may say that colitis constitutes a much greater threat to the health and occasionally to the life of the gravid mother. While the question of therapeutic abortion is often raised in the colitis case, that issue is rarely a factor of debate in the ileitis case. In both ulcerative colitis and ileitis, the proportion of abortions, miscarriages and stillbirth does not exceed those in the control population.

Chapter 8 Radiographic Diagnosis of Regional Ileitis, Ileo-Jejunitis and Ileocolitis

by Richard H. Marshak, M.D.*

SEVERAL INVESTIGATORS have divided the roentgen finding in this disease into acute, subacute and chronic stages. Since the classical form of regional enteritis is that of a low grade inflammatory process with episodes of acute exacerbation, it is difficult to identify such a clear-cut pattern. Acute granulomatous regional enteritis has been described, but the determination of the precise time of onset of this disease is unusually difficult.

Roentgen demonstration of proximal and distal extension of the disease process, despite repeated examinations extending over a period of many years, has not been observed. The maximum length of involvement was determined on the initial roentgen studies. This is not true after exclusion operations when recurrent disease is not uncommon.

One of the prominent features of the disease is the development of stenosis with obstruction. Therefore, roentgenologically, the cases may be divided arbitrarily into stenotic and nonstenotic groups. It is difficult to classify these groups as early and late, since the majority of cases may continue without stenosis for many years. Again, division into active and inactive seems inappropriate, as the patient with long segments of stenotic bowel may also exhibit considerable evidence of clinical activity manifested by fever, diarrhea and abdominal pain.

Nonstenotic Phase The roentgen findings closely parallel the pathologic features. The earliest mucosal alterations are blunting, flattening and thickening of the valvulae conniventes. The folds are arranged in a fairly regular, symmetrical, parallel fashion and, as progression occurs, may become thicker, irregular and partially fused (fig. 27). The bowel lumen becomes irregular in width. These changes are due to the inflammatory submucosal and mucosal thickening. When ulceration

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Are also in Radiology Museum Hospital New York City



FIG. 7 The folds are thickened blunted and in some areas fused. The contour is irregular. There is rigidity and separation of the loop of intestine. The intestinal loops appear straightened or uncoiled. Diagnosis: Nonstenotic type of regional enteritis.

occurs a more characteristic pattern is produced. Longitudinal streaks of barium recognizable as ulcerations appear (fig. 28). As the thick blunted folds of mucosa are further destroyed cobblestoning may be noted (fig. 29). This specific pattern is more common in the jejunum probably because of the thicker valvulae in this region. Ulceration continues at the expense of the intervening islands of mucosa replacing the cobblestone pattern by an irregular network of interlacing streaks of barium. The appearance at this stage has no uniformity or symmetry and is hazy and reticulated. Denudation of the mucosa is usually incomplete leaving behind islands of inflamed mucosa which produce multiple smooth defects of varying size (fig. 30). Their prominence is increased by the narrowing of the bowel lumen which is due to beginning cicatricial contraction that occurs at this stage. Finally one may see the radiologic image of a uniform rigid castlike tube filled with barium and present



FIG. 28 Longitudinal view of barium sulfate ulceration are seen. The contrast is good with some spasm and paucity of the loops of intestine. Diagnosis: Non-toxic type of regional enteritis.

ing no mucous membrane pattern. This is similar to ulcerative colitis and represents the stage when scarring and regeneration of an atrophic mucosa is progressing (fig. 31). As scarring proceeds the transition to the stenotic phase occurs. An uncommon but striking finding is the presence of large inflammatory polyps (fig. 32). Ordinarily the polyps are much smaller. Carcinomatous transformation of these polyps has not been observed. Coincident with changes in the mucosa other characteristic roentgen features occur. The bowel lumen reveals varying degrees of narrowing (fig. 27). Early the submucosal thickening and associated spasm are responsible for the narrowing of the lumen. Later as fibrosis occurs the narrowing is more marked and leads finally to the stenotic

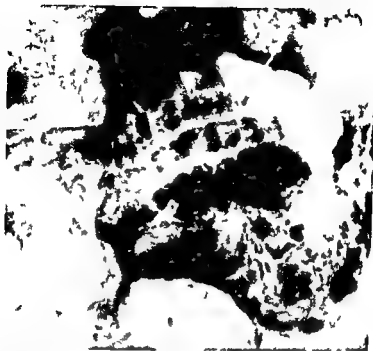


FIG 29 A cobblestone pattern is noted. In other areas the folds are thickened and blunted. The loops of intestine are moderately rigid and somewhat separated. Diagnosis: Non-tenotic type of regional enteritis.

stage (fig 34). In the early stages rigidity of the contour and mucosal pattern is incomplete. Some flexibility or dynamic activity is evident in the change in contour and mucosal pattern during successive roentgenograms (fig 27). Later the roentgen appearance is fixed and unvarying (figs 31-34). Flexibility is lost. Also early in this disease the normal serpentine or coiled pattern of the loops of small bowel disappears. The diseased segments appear to be straightened and rigid (figs 27-30). This finding is probably the result of loss of flexibility of the bowel wall and mesentery as well as longitudinal shortening due to spasm.

Frequently the loops of intestine appear to surround a mass (fig 28). Although this may be due to an abscess resulting from perforation more often it is secondary to the indurated mesentery associated with the marked increase in the mesenteric fat and the enlarged lymph nodes. Because the intestine is diffusely ulcerated and contains exudate and



FIG. 30 The rigid type spasm of the ileocecal junction is a small filling defect due to inflammatory polyps and eccentric skip area. Diagnosis: Nonstenotic form of ileocecal junction.

excessive secretions and the barium does not adhere to the walls the silhouette of the intestine may be hazy. Despite the increase in intestinal content the barium mixture remains fluid and homogeneous. Agglutination, clumping or formation of masses of barium is not found in regional enteritis as contrasted with the findings in the so-called true pattern. Segmentation such as is characteristic of sprue has not been observed. When unequivocal segmentation occurs the diagnosis of regional enteritis should be suspected. Skip areas (fig. 30) that is segments of normal intestine intervening between diseased segments represent another characteristic feature. The length of a skip area may vary from a few inches to several feet. The extent of involvement on a



FIG 31 The loops are rigid and markedly separated. The mucosal pattern appears cauliflower-like. Several small filling defects are noted due to inflammatory polyps. Diagnosis: Nontenotc type of ileojejunitis.

roentgenogram may be quite accurately determined in most cases since the transition of disease to the normal intestine is fairly abrupt. An outpouching of the mucosa between the thickened fold (fig 33) occurs in some cases, creating an appearance suggesting large diverticula. This



FIG. 32 Large filling defects. There is a moderate degree of rigidity with loss of narrowing. The loop is everted. Diagram. No stenotic type of lesion.

is peculiar in that it seems to affect one side of the intestine and not the other. These pseudodiverticula probably represent small eccentric skip areas.

Stenotic Phase In the stenotic stage many of the rigid loops described previously become constricted to a remarkable degree. These stenotic segments resemble rigid pipestems (fig. 35-37). This appearance is due to a marked thickening and contraction of the wall of the small intestine. The stenosis may extend through 1 or 2 cm. or over long segments. With severe narrowing dilatation of the proximal intestine may be marked. In many instances it is difficult to state whether or not intrinsic disease is present in a dilated area. Very often disease is present when a loop of dilated intestine exists between two points of



FIG 31 The loops are rigid and markedly separated. The mucosal pattern appears cauliflower-like. Several small filling defects are noted due to inflammatory polyps. Diagnosis, Nonstenotic type of ileocejunct.

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FIG 34 Same patient as in figure 3^o ten years later. At this time the lumen of the intestine is narrowed. The filling defects previously described are not as prominent. There is no evidence of an inflammatory mass. Diagnosis: Stenotic phase of ileocecalitis.

The loops are rigid and remain in a constant position from film to film. Fistulas usually involving the distal ileum are frequent (fig. 41). Occasionally these are very difficult to demonstrate especially when dilated loops of intestine produce overlapping. The fistulas may extend to and penetrate the abdominal wall.

In general the roentgen findings in regional enteritis are as described; however, there are certain characteristics which are peculiar to the area of involvement.

Ileum: The most frequent site of involvement of the small bowel with regional enteritis is the terminal ileum (figs. 39-40).

The terminal ileum which has come to be identified as the pathog-



FIG 33 The diseased loops of intestine are moderately rigid and separated. The folds are thickened and blunted. Pseudodiverticula are present. Diagnosis: Nonstenotic type of regional enteritis.

constriction. On the other hand, when there is a single area of constriction with proximal dilation, disease may not be present in the dilated segment. However, because of retained secretions, secondary inflammatory changes, tension ulcers, and muscular hypertrophy, the appearance of the dilated loops may be confused with the alterations seen in regional enteritis. This distinction is of great importance when considering surgical therapy. Some cases have not undergone operative intervention because the surgeon was of the opinion that the entire intestine was involved. Extreme dilatation of the intestine for long segments is rarely associated with intrinsic granulomatous disease.

Many of the roentgenographic phenomena observed in the nonstenotic phase of the disease are again noted in the stenotic phase. The mucosal pattern is usually reticulated or castlike. Small filling defects, inflammatory polyps, irregularly distributed throughout the diseased segments, are noted. Skip-areas and wide spacing between the segments of intestine are more striking (figs. 35-38).

nition of the fact that the string sign does not always indicate marked fibrosis and stenosis is important since exclusion operations during the stage of marked ulceration and activity have been followed by a high degree of recurrence.

Because of the marked ulceration, fistulas and perforation (fig. 41) thickening of the mesentery and separation of the loops of bowel are more frequent in the distal ileum than in the remainder of the small



FIG. 36. The distal jejunum and proximal two thirds of ileum show large area of narrowing alternating with areas of dilatation. The mucosal pattern in the stenotic areas is reticulated. The loops of intestine are widely separated and displaced. Significant stenosis of ileocecal junction.

bowel. A possible explanation of the marked ulceration in the distal ileum may be the higher bacterial content in this area. Deformity of the cecum and ascending colon is not unusual with involvement of the terminal ileum. The deformity is most often due to the intense inflammatory process in the mesentery and to fistulas arising from the terminal



FIG 35 The mucosa is caustlike with inflammatory polyps The affected loop is rigid and narrowed with an associated inflammatory mass - Diagnosis Early stenotic stage of ileo jejunitis

nomonic roentgen manifestation of regional enteritis is most frequently noted in this area. It has been described as a thin linear shadow suggesting a frayed cotton string in appearance (fig 39). The cause of the string sign is incomplete filling due to irritability and spasm associated with marked ulceration and may be seen in both the nonstenotic and stenotic phase of this disease. Repeated spot films will demonstrate the fact that some distensibility is still present in this segment (fig 40). The bowel proximal to the string sign may or may not be dilated depending on the stage of the disease. In the nonstenotic phase the proximal intestinal lumen is generally not dilated despite the marked narrowing associated with the string sign indicating the importance of spasm in producing this characteristic appearance. This spasm is usually inconstant. When persistent temporary proximal dilation can occur with symptoms of obstruction. In the stenotic phase there is constant proximal dilatation which may be accentuated by spasm secondary to ulceration. Despite the narrowing complete intestinal obstruction is rare. The recog-



FIG. 33. Long rigid narrowed segments resembling pipe stems with a large inflammatory mass. Diagnosis: Stenotic phase of regional enteritis.

vention until recently has been rare and long follow up of the natural course of the disease has been possible. The transition from the non-stenotic to the stenotic stage could be observed. In the average case the interval was approximately four to five years. In the stenotic phase the proximal bowel may become hugely dilated. In these cases unless adequate amounts of barium are administered the exact ulcerations may not be identified. Partial intestinal obstruction in this group of patients is common; however complete intestinal obstruction has not been observed.

It is of interest that many of these patients with extensive involvement of the intestinal tract despite numerous episodes of partial intestinal obstruction can maintain an adequate nutritional status (fig. 43).

Jejunum. Twelve cases isolated to the jejunum were studied. In every patient there was marked stenosis. Three types of stenosis have been recognized: a single area of stenosis with proximal dilatation; a



FIG 37 The entire small intestine is involved with alternating areas of constriction and dilatation. There is separation of loops of intestine. The mucosal pattern in some areas is castlike and in others reticulated. The intestinal loops appear to surround the mass. Diagnosis: Stenotic phase of regional enteritis.

ileum and extending into the right side of the colon (fig. 42). In most of the cases the granulomatous inflammatory process ends abruptly at the ileocecal valve.

Regional enteritis involving the terminal ileum does not always produce marked ulceration. There are many instances in which the inflammatory process is minimal. In these patients the roentgen findings reveal slight rigidity, slight lack of distensibility and slight serration of the contour of the bowel.

Ileo jejunitis. The distal half of jejunum and proximal half of ileum are characteristically involved (figs. 29, 31, 32, 34). Skip areas are frequent. Large inflammatory polyp may be noted (fig. 32). Ulceration is not as marked as in the terminal ileum and fistula formation is less frequent. Because of the extent of involvement operative inter-



FIG 40 Same pat nt as in fig e III a few minutes later illustrating distention. Not also possible

in the remainder of the small bowel. Sidetracking operations have been successful in every case but one, again pointing to the fact that recurrences are more frequent when the operation is performed in the presence of marked ulceration and fistula formation. Isolated jejunitis in the



FIG. 39 String sign in regional enteritis

second form with two areas of narrowing and marked dilatation of the bowel between simulating a closed loop obstruction (fig. 44) and a third type with multiple stenotic segments and intervening dilatation of the intestinal loop (figs. 45-46). The length of stenosis has been short varying from one to three inches. Ulceration is minimal. Fistula formation is uncommon and the thickening of the mesentery is not as marked as



FIG 40 Same patient as in figure 33 a few minutes later. Illustrating distention. Note also position of cecum.

in the remainder of the small bowel. Sidetracking operations have been successful in every case but one, again pointing to the fact that recurrences are more frequent when the operation is performed in the presence of marked ulceration and fistula formation. Isolated jejunitis in the

nonstenotic stage has not been observed. These patients apparently have minimal symptoms for many years and are not investigated until partial obstruction supervenes.

Duodenum Four cases were studied. The findings in the duodenum are essentially similar to those in the jejunum (fig. 47). Moderate stenosis is present and the ulcerated areas are seldom deep or marked. Two of these patients have an associated terminal ileitis (fig. 48).

Recurrent Ileitis In general the recurrent lesion acts similarly to the original process. The earliest roentgen findings are again thickening



FIG. 41 Terminal ileitis with numerous sinuses and fistulas. Some of these extended into the urinary bladder.

and blunting of the fold, progressing through the many stages through the stenotic phase. Fistula formation appears to be less frequent. The length of the lesion has no effect on the recurrence rate. The colon is rarely invaded and the usual site is the new terminal ileum (figs. 49-50). Recurrences also appear to be more frequent in those patients in whom the initial lesion reveals marked ulceration with fistula formation. Many patients with early recurrent lesions may be completely asymptomatic.

Healing in Regional Enteritis While spontaneous remissions and clinical improvement following a variety of operative and conservative



FIG. 42. Terminal ileitis with large fistula between terminal ileum and ascending colon.

therapies: frequently observed there is not a great deal of information demonstrating radiologic and pathologic healing. Patients who undergo reexploration following ileocolostomy can show a remarkable degree of healing of the involved segments of bowel and mesentery. The ulcerations may disappear and the fistulae close. Demonstration of improvement without operation is rare in this series. Three cases, however, have been observed where remarkable roentgen changes indicating healing occurred (figs. 51-52). Despite these instances of improvement, the large majority of cases demonstrates the disease to be continuous (figs. 32-34). Many years, however, may elapse before stenosis supervenes. It should be pointed out that secondary changes may occur in patients who are clinically improved, notably stenosing lesions and permanent loss of the normal small intestinal structure. These changes are due to healing with scar formation.

Regional Enteritis with Involvement of the Colon. In most cases of regional enteritis the roentgen alterations appear to end abruptly at



FIG 43 Entire ileum involved with regional enteritis. Lesion unchanged during 8 year observation.

the ileocecal valve. In a few patients involvement to the hepatic flexure was noted (fig 53). In four instances skip lesions from ileum to transverse colon were seen and in one patient there was involvement as far as the sigmoid. The roentgen alterations in the colon were remarkably similar to the lesion in the ileum and usually revealed marked narrowing of the bowel lumen. In the patient where the disease extended as far as the sigmoid it was impossible to differentiate the colonic alteration from ulcerative colitis.

Combined Disease. Regional enteritis may be associated with ulcerative or segmental colitis. The characteristic findings of regional enteritis are unaffected by the inflammatory disease in the colon whether ulcerative or granulomatous and present the alterations described previously consisting of narrowing of the intestinal lumen, rigidity, ulcer



FIG. 44 The mid jejunum is an old with alternating areas of constriction and dilatation. One loop of jejunum is abnormally dilated. Diagnosis: Stenosing jejunitis.

ation of the mucosa, inflammatory polyps, skip areas, fistula, and separation of the involved intestinal loops.

In the majority of cases the inflammatory process is confined to the distal part of the ileum. In some cases diffuse jejunoileitis was present. It is important to differentiate regional ileitis from so-called backwash ileitis which may be associated with ulcerative colitis. In backwash ileitis the narrowing of the intestinal lumen is not as marked as when there is granulomatous involvement. The mucosa usually presents minimal ulceration, fistula formation is rare, skip areas are uncommon, and marked separation of the intestinal loops is not usually observed (fig. 54). In some cases of backwash ileitis, however, the ulceration of the mucosa



FIG 43 Entire ileum involved with regional enteritis. Lesion unchanged during 8 year observation

the ileo cecal valve. In a few patients involvement to the hepatic flexure was noted (Fig. 53). In four instances skip lesions from ileum to transverse colon were seen and in one patient there was involvement as far as the sigmoid. The roentgen alterations in the colon were remarkably similar to the lesion in the ileum and usually revealed marked narrowing of the bowel lumen. In the patient where the disease extended as far as the sigmoid it was impossible to differentiate the colonic alteration from ulcerative colitis.

Combined Disease Regional enteritis may be associated with ulcerative or segmental colitis. If the characteristic findings of regional enteritis are unaffected by the inflammatory disease in the colon whether ulcerative or granulomatous, it is recent the alterations described previously consisting of narrowing of the intestinal lumen, rigidity, ulcer



FIG 46 Greatly dilated segment of jejunum proximal to an area of narrowing in distal jejunum. Diagnosis: Stenosing jejunitis.



FIG 45 Constricted segments starting at ligament of Treitz alternating with areas of dilatation in jejunum. There is considerable dilatation of the duodenum. The mucosal pattern in constricted areas appears castlike. Diagnosis: Stenosing jejunitis.

is marked producing sufficient spasm as to result in the formation of the 'string sign'. This finding, however, is unusual and the degree of narrowing and rigidity usually seen with regional enteritis associated with proximal dilatation is absent.

When the lesion in the colon is diffuse the roentgen alterations are similar to those usually identified with diffuse nonspecific ulcerative colitis. In the case where there is an associated segmental or granulomatous colitis the findings are usually limited to the right side of the colon; skip areas are not infrequent; inflammatory polyps are larger and there is more marked narrowing of the bowel lumen.



FIG 46 Greatly dilated segment of jejunum adjacent to an area of narrowing in distal jejunum. Diagnosis: Stenosing jejunitis.



FIG 47 Regional enteritis involving the second portion of the duodenum
The terminal ileum was also involved



FIG 43 Regional ileitis involving the stomach. The terminal ileum was also involved.

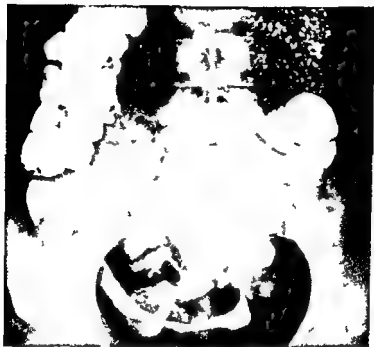


FIG 51 Terminal ileitis



FIG. 5 Same patient one year later. Note marked improvement in the appearance of the terminal ileum. The findings at this time are minimal.



FIG 53 Regional enteritis with extension into the colon to the hepatic flexure



FIG. 54 Right sided ulcerative colitis with involvement of the ileum (back wash letter 2)



FIG 53 Regional enteritis with extension into the colon to the hepatic flexure



FIG. 56 Status post colectomy for ulcerative ileitis with ileostomy. Inflammatory disease involving distal ileum (nonganglionic).



FIG 55 Status postileosigmoidostomy with recurrent disease in rectum sigmoid and adjacent ileum

or more of these signs and symptoms should suggest the consideration of ileitis. Diarrhea alone, diarrhea plus fever, diarrhea with fistula, an abdominal mass with fever, an intestinal or perirectal fistula, or any combination of such symptoms and physical findings is suggestive. An illustrative case in point is worth quoting because of its significance.

P.B. (Serial No 197) Male, age 39 years. For many years he had suffered with mild diarrhea. Eight years ago he had been operated on for a rectal fistula. Subsequently he had lost 59 pound, complained of abdominal cramps and persistent diarrheal movements. The physical examination was negative except for slight tenderness over the cecal area of the abdomen and suggestive clubbing of the fingers. The rectal and sigmoidoscopic examinations were negative. The radiographic examinations, barium enema and barium meal, were reported as negative except for some evidence of a spastic colon. The terminal ileum was well visualized, appears somewhat irritable in its distal portion, but fills well and is distensible. The report to the referring physician stated that although the diarrhea, fever, and the past rectal fistula strongly suggested ileitis, the absence of confirmatory radiographic evidence made such a positive diagnosis impossible. It was urged that the patient be carefully observed for future developments. Six months later the patient developed a fistula from the ileum to the sigmoid. At operation a regional ileitis was discovered involving 5 feet of ileum proximal to the ileocecal valve. An ileo-transverse colostomy with transection of the ileum resulted in cure.

The significance of the perianal fistulas cannot be overlooked. In former years such fistulas either were regularly regarded as being tuberculous in nature or were suspected of a tuberculous origin. Mumery in 1923 considered at least 15-20 per cent of perirectal fistulas to be of tuberculous pathogenicity. In a survey of anal fistulas summarizing 600 cases, Jackman and Bue found 87.8 per cent negative for tuberculosis. In the true tuberculous fistulas primary affects elsewhere in the body, usually the lung, were always demonstrable. This reversal in the viewpoint of the relationship of tuberculosis to anal fistulas is due in large part to the increasing role which ileitis and colitis play as etiologic factors in the incidence of such perirectal complications.

It is particularly important to have sufficient mental fortitude to

Chapter 9 The Diagnosis of Regional Ileitis

THE DIAGNOSIS of regional ileitis is essentially a clinical one based upon the characteristic subjective symptoms and the physical findings. The x ray diagnosis is valuable as confirmatory evidence and allows for anatomic interpretation of the lesion. It is a grave error to think of ileitis as an obscure disease difficult or impossible to diagnose. Ileitis has clear cut subjective and physical features which when combined spell out a succinct clinical diagnosis. The combination of diarrhea, fever, anemia and fistulas internal or external with or without an abdominal mass with or without radiographic confirmation means a possible or a probable diagnosis of ileitis. The negative sigmoidoscopy rules out the usual case of ulcerative colitis 95 per cent of which cases give a distinct pathologic sigmoidoscopic picture. The remaining possibility is a right sided segmental colitis to be differentiated from regional ileitis. Segmental colitis may and does have anal complications and rectal fistula but no fistulas to the abdominal wall and no internal fistulas or intra abdominal masses. To recapitulate the diagnostic significance of the symptoms and signs of ileitis:

- 1 The diarrhea is the most common feature being present in 95.5 per cent of the cases.

- 2 Fever is frequent and significant but the majority of the long standing low grade cases are afebrile.

- 3 Anemia may be so moderate as to be insignificant a hemoglobin reading below 65-70 per cent is of value.

- 4 Loss of weight is significant but may not be extensive. An abdominal mass may be present but most frequently is absent.

- 5 Fistulas internal external and perirectal are the most nearly pathognomonic manifestation of the disease particularly when associated with diarrhea and with the other positive signs and findings of ileitis.

The radiographic study is exceedingly important when positive or a negative finding does not necessarily nullify a clinical tentative diagnosis of ileitis. Any one symptom especially any combination of two

4 years during which time because of a soft systolic mitral murmur over the precordium the case had been considered as one of chronic heart disease or subacute bacterial endocarditis in spite of repeated negative blood cultures. Sprague et al report a case of long standing fever in a girl of 15 years of age who presented the clinical picture of an irregular fever with temperatures ranging between 101 and 104 F with polyarticular rheumatic like arthritic manifestation and perirectal abscess the whole clinical picture being due to regional ileocolitis.

The significance of the cardiac murmur may be overemphasized. At least 5 cases in this series had had rheumatic fever and bore residual systolic mitral or aortic murmurs. Add to the old rheumatic cardiac murmur a low grade fever and the possibility of ileitis or segmental colitis is rarely considered. This is all the more important because in one case in this series an acute endocarditis actually occurred as a complication while the patient was under observation. A young woman with recognized regional ileitis was under observation preparatory to operation. An increased degree of fever was associated with the development of a systolic murmur at the cardiac apex the murmur was heard with daily increasing intensity a low rough murmur was audible and was transmitted to the mitral area. A blood culture was negative at the height of the fever. Penicillin was instituted the fever subsided in 7 days and the cardiac murmur ceased to be audible. The patient was later successfully operated on for regional ileitis. No further cardiac manifestations occurred.

The larger and sometimes smaller joint of the hands or feet may be implicated in diarrheal diseases the so called "arthritis dysenterique" but the significance of the arthritis as an intestinal manifestation is usually overlooked in favor of a diagnosis of rheumatic fever with joint involvement.

The mild or moderate eosinophilia that frequently accompanies ileitis and colitis may suggest and be confused with periarthritis nodosa.

The eye complications which occur occasionally in ileitis but more commonly in ulcerative colitis again are usually overlooked and are classified in the tuberculous or rheumatic category (Sprague et al). Ophthalmologists of wide experience are conscious of the fact that inflammatory lesions of the eyes are not uncommon complications of intestinal disease. Iritis, iridocyclitis, keratitis, corneal ulceration and phlyctenular conjunctivitis all constitute focal manifestations of intestinal diseases.

sustain the diagnosis of at least probable ileitis even though many significant clinical features are missing and the x ray diagnosis is negative. On several occasions one has been saved from a blatant error by including in the provisional negative diagnosis at least the possibility of ileitis. The following experience is illustrative.

The case was reported as nervous diarrhea irritable colon but the proviso was added of a possible ileitis. Five years later the symptoms flared up and now exploratory laparotomy showed regional ileitis with an ileo sigmoid fistula. Not that every case of diarrhea should be classed as a possible ileitis but the association of diarrhea with a fistula a mass fever or anemia or any such combination calls for diagnostic caution and acuity.

The low grade fever of regional ileitis is often overlooked by general internists who are likely to pay little attention to mild diarrhea or to the complaints of occasional front abdominal pain. The patient may not consider two or three loose bowel movements as diarrhea the abdominal pain may be minimal and no positive physical signs may be discoverable. The cases of ileitis with low grade fever are usually confused with brucellosis or undulant fever particularly when a low titer agglutination against the *Melitensis* organism has been reported. Many a case of ileitis has been overlooked because of a positive agglutination of 1:40 or 1:80 against brucella. One such case was even published in medical literature in this country (Sproull) as a case of undulant fever with unusual intestinal change. This before the first description of ileitis as a clinical entity. Years later exploratory operation and resection of the ileum revealed the true nature of the disease as one of ileitis with low grade fever the doubtful low grade agglutination titer against brucella having only confused the diagnostic issue.

Ileitis which presents itself as a case of continuous low grade fever with low leukocyte count occasional joint involvement clubbing of fingers or eye complication especially when a heart murmur is present is likely to be overlooked this is particularly true when the minimal diarrhea which is the actual key to the diagnosis is ignored. All of these manifestations of a generalized disease are common to both ulcerative colitis and ileitis omit the diarrhea and the general symptoms resemble brucellosis rheumatic fever subacute bacterial endocarditis lupus erythematosus dieminitis or Libman Sachs disease. Rosenblate Goldsmith and Straub cite a case of regional ileitis unrecognized for



FIG. 11. Hodgkin's Disease simulating ileitis.

Intra abdominal Hodgkin's disease by its fever and low leukocyte count and its possible intestinal involvement may simulate ileitis. Multicentric intestinal lymphosarcoma with its characteristic areas of intestinal dilatation its hemorrhage fever perforation and rapid wasting may be confused with ileitis. Both Hodgkin's disease and intestinal sarcoma are intensely malignant and progressive diseases with early fatal issue in contrast to the more mild and low grade continuous course of chronic regional ileitis (figs 5/ 68).

The string sign of the terminal ileum may be simulated by hyper

Differential Diagnosis

When a suggestive string sign is present or when a disarrangement of the pattern of the intestinal mucosa is noticeable in the roentgenograms various other possible intra abdominal diseases come into consideration in the differential diagnosis. When the upper ileum and the jejunum show puddling and segmental delays as well as disturbed mucosal patterns sprue and the vitamin deficiency diseases deserve close notice. Here the differentiation between sprue and ileo jejunitis is often difficult (fig 71)



FIG 57 Lympho sarcoma simulating ileitis

the liver McLeod adds 2 cases to 283 reports in the literature (1944) intestinal obstruction in the terminal ileum and organ metastases were commonly observed Dockerty and Ashburn in a review of the literature describe carcinoid tumors (so-called) of the ileum They detail 30 cases of carcinoid of the terminal ileum 11 of which had metastasized locally or distally small orange submucosal nodules were arranged linearly with a minimal degree of ulceration Regional lymph nodes were involved in 11 cases in 5 metastases to the liver were present suggesting a low grade type of carcinoma virulence

Endometrial transplants on the serosa of the terminal ileum with or without invasion of the intestinal walls occasionally may be confused with ileitis the string sign is almost identical The intestinal bleeding with the menses may if present suggest the true nature of the lesion A case of endometriosis as a cause of intestinal obstruction has been described (McGuff et al) in which the segment 5 cm proximal to the ileocecal valve was involved by endometrial transplant The clinical picture resembled in general a case of regional ileitis with intestinal obstruction

Enterogenous cysts about the ileo-cecal angle are exceedingly rare but may simulate roentgenographically the constriction of terminal ileitis (Rosenberg)

Actinomycosis of the intestinal wall with abdominal wall fistulas may simulate ileitis the finding of the characteristic ray fungus in the discharges from the fistula will save much confusion and often embarrassment The possible confusion between ileitis and sarcoidosis has already been discussed (page 13) Sarcoidosis of Boeck involving the small intestine as a granulomatous lesion was described by Watson and his associates the identity of ileitis and sarcoidosis was even suggested by Hadfield Snapper however has made the point that he never encountered a case of sarcoidosis with a lesion of the intestine nor have his many cases of ileitis ever shown sarcoidosis Blackburn states that in ileitis there is no record of swelling of the fingers and toes lymphadenopathy or the uveoparotid syndrome such as is observed in typical sarcoidosis Sarcoidosis is a generalized disease affecting the reticulo-endothelial structural system Intestinal involvement by sarcoidosis without generalized implication of other organs would be difficult to accept

Impairment of the blood supply to the intestinal tract may reproduce a clinical picture simulating acute or chronic regional ileitis the radiographic picture of such a vascular lesion may be very confusing Such

plastic ileo cecal tuberculosis carcinoid of the terminal ileum endometriosis of the terminal ileum enterogenous cysts about the terminal ileum and actinomycosis intestinal

Primary intestinal tuberculosis as a manifestation of bovine infection is exceedingly rare in a complete survey of all the postmortem and surgical pathologic material at the Mount Sinai Hospital over a period of 15 years only 4 cases of primary intestinal tuberculosis were found to have survived a critical analysis (Crohn and Yarnis) In 2 of the 4 cases the ileum was the site of typical military tuberculosis tubercle bacilli were found in the sections of the histologic studies All other cases were those of ileo cecal or ileal tuberculosis secondary to open lesions in the pulmonary areas with caseating cavity formation and positive sputum or positive gastric residue findings for tubercle bacilli

Cases of regional ileitis regularly have negative chest finding by physical examination and by radiographic study Cases of secondary intestinal tuberculosis have strongly positive chest plates with evidence of cavity formation and with positive sputum findings That intestinal tuberculosis can simulate exactly the string sign of ileitis has been amply demonstrated (Crohn and Yarnis) This point has also been emphasized by Connell Blackburn found the Mantoux test negative in 19 of the 22 case and x rays of the chest uniformly negative in regional ileitis

Argentaphilic carcinoid tumors infiltrating along the mucosa of the terminal ileum represent a favorite site for that lesion and can simulate the clinical picture and the radiographic string sign of ileitis In one case in my experience the terminal ileum was resected under the supposition that it represented a case of ileitis the gross specimen was passed from hand to hand and was accepted as one of ileitis by many long-experienced in handling such surgically resected specimens Only on histologic study was the true character of the lesion identified as one of carcinoid tumor of the terminal ileum with metastase to the mesenteric lymph nodes

Up to 1939 237 cases of argentaffine tumors of the small intestine had been reported in the literature obstruction occurred in 24.4 per cent of these Pennington and Priestly report 4 cases of carcinoid tumors of the terminal portion of the ileum invading the mesentery The abdominal mass involved several loops of the terminal segments of the ileum The lesion was malignant several metastatic tumors being present in

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circulatory disturbances may be secondary to a strangulated hernia or to volvulus or it may result from arterial occlusion venous thrombi or infarctions. If such a pathologic process is limited to one segment of the small intestine and if spontaneous healing does ensue the radiographic representation may be one of isolated string sign or may indicate a segmental area of stenosis simulating true regional ileitis (Wolf and Marshak)

Chapter 10 Prognosis in Regional Ileitis Under Medical or Conservative Treatment

IN THE 1949 EDITION of this monograph only 13 out of a total of 222 cases of chronic regional ileitis were observed to undergo spontaneous healing or cure. At that time some question was necessarily raised as to what constituted cure and what the durability was of such a so-called cure or self-healing. This was a logical source for skepticism since the follow-up of surgically treated cases showed late recurrences to take place as long as 9, 14 or 17 years after what seemed to be a successful operation. If the late surgical recurrences created legitimate doubt as to durability of cure, how much more so would a follow-up of medically treated cases raise the same scientific question of durability of long-term beneficial results?

What constitutes so-called cure in regional ileitis? Not the roentgenographic picture alone for clinical improvement and disappearance of symptoms may be thoroughly achieved while the radiologic evidence may persist in showing string sign deformity and irregularity of loops of small bowel. Can a true chronic granulomatous lesion of the intestine ever heal without lasting deformity in the roentgen films any more than a true penetrating duodenal ulcer with crater formation can ever return to the picture of a normal duodenal bulb as radiographically demonstrable?

The return of general well-being, the restoration of weight loss, the cessation of anemia and the reduction or disappearance of diarrhea constitute marked improvement in the subjective symptoms. Add to this an inability to palpate a previously demonstrated mass and surprisingly even the healing of perirectal fistulas and one may be pardoned for regarding such a case as an instance of cure provided that the factor of time in the follow-up is always borne in mind. By cure, if that term can be employed in such long-standing disease, I meant clinical betterment, cessation of subjective symptoms and objective findings—not necessarily a return to a normal roentgenographic picture of the small bowel.

By improvement one surmises a marked alleviation of symptoms a return to good nutrition diminution of diarrhea and ability to follow one's daily tasks and participate in family and public social activities

In this series of 542 cases of regional ileitis there were 111 cases roughly 20 per cent that were observed and followed under conservative observation over a course of years. The conclusions in this series were unfortunately incomplete since 26 of the patients were lost to follow up. The results to date of the remaining 85 cases may be tabulated as follows

TABLE 9
MEDICAL FOLLOW UP (85 CASES)

Years	Well	Improved	Unimproved	Died
1	8	6	7	2
2	8	2	4	0
3	12	1	3	0
4	7	2	0	0
5	3	3	0	0
6-10	9	1	2	0
11-15	2	0	1	0
16-25	2	0	0	0
Total	51	15	17	2

At first one is surprised at the apparent large number of so called instances of cure. 51 out of 542 cases or roughly 9.4 per cent in the earlier series of 1949 there were only roughly 5 per cent of spontaneous cure. This improvement in figures may be due to two factors: one a reluctance to operate as freely and as early in the course of the disease as in the previous years of surgical enthusiasm the other a possible improvement in medical care: more diligence and patience in instituting conservative therapy and possibly or probably the extensive use of steroid therapy over longer periods of trial. Note also that 15 cases were regarded as improved and 17 as unimproved and yet surgery was withheld in an attempt to protract the period of conservative therapy and thus avoid more drastic operative steps.

In the last decade we have been passing through a period of warrantable skepticism regarding end results of surgical intervention. The larger numbers under conservative management reflect the current doubts as to the long range curative effects of operative interference. And yet 51 cases observed over a follow up of from 1 to 25 years appeared to be cured or free of symptoms and returned to health and well being.

The true proportion is restored however when it is noted that the remaining 431 cases of this larger series had been subjected to surgical intervention and that these cases all represent the failures of conservative management. Nevertheless all in all roughly 10 per cent (actually 9.4 per cent) of ileitis cases do respond to medical therapy, this figure small as it is does constitute a plea for patience in the treatment of such cases and does seem to substantiate the opinion of those who are reluctant to submit to operation every case of ileitis as soon as the diagnosis is established.

In an occasional instance (5 cases) in this series cure was confirmed by the disappearance of roentgen evidence of the disease. These cases are however very rare and exceptional.

The duration of the cure as noted in the follow up is 71.0 of interest while the majority of favorable cases have been observed for only 1 to 5 years there were 9 cases of cure that had lasted 6 to 10 years and 4 cases followed for 10 to 25 years that had remained well. This was an interesting and admittedly a surprising observation. Good as it is it is only suggestive (but nonetheless encouraging) to those who advocate conservative therapy but it does not justify Barger¹⁴ who in a recent paper emphasizes an allergic etiologic factor in the disease and states that he and his colleagues have become very conservative in the surgical treatment of regional enteritis.

In the prolonged observation of cases of regional ileitis extended over the course of years deaths are not unusual. In our series of 542 cases there were in all 28 fatalities. Twelve of these were immediately operative or post operative the remaining 16 cases died while under prolonged medical observation just half of these due to the ileitis per se the other half (8 cases) due to intercurrent disease.

TABLE 10
MORTALITY UNDER MEDICAL OBSERVATION

Cause of Death	No. of Cases
Myocardial Infarction	1
Coronary Disease	3
Cerebrovascular accident	2
Brain Tumor	1
Steroid Ulcer with fatal hemorrhage	1
Malnutrition due to ileitis	8
Total	16

Considering that the follow up of the *c* individuals extended over a period of from 1 to 25 years (table 9) it will be seen that only 8 of the 542 cases died of the disease itself the remaining fatalities being attributable either to surgical intervention or to causes foreign and not directly attributable to the pathologic intestinal process

Chapter 11 Medical Therapy, Conservative Palliative Treatment of Regional Ileitis

General Directions

THE PHYSICIAN should direct his patients to adhere to the following regimen

Live in an atmosphere which is peaceful Try to control anxiety worry or mental upset Plan every day so as to have a rest period and as much quiet as possible

Fresh air and sunbath are fine aids to a quick recovery

No competitive games or strenuous exercise Plan recreation which does not produce nervous tension or great fatigue no tennis match no card games for money no horse back riding

Have a full and highly nutritious diet by eating three regular meals plus light mid morning mid afternoon and evening lunch That is eat once every two and a half hours throughout the day and little or nothing after 10 p m

Diet

A bland low fat protein rich diet should be instituted Abundant proteins and the liberal use of carbohydrates are necessary to maintain nutrition against the wasting of the disease and against hypoproteinemia that may ensue as a result of protracted fever and diarrhea Coarse fruits and vegetables should be eliminated soft vegetables well cooked should be pureed or passed through a collander Fruit juice may be allowed in limited quantities soft fruits such as bananas apple sauce soft pears and ripe peaches are allowable The greatest attention is paid to meats and fishes cheese protein milk and eggs as food with high nitrogen content The diet should be supplemented by the administration of protein calcium hydrolysate or sustagen with high amino acid content 6 8 or 12 ounces a day taken in milk water fruit juice cocoa substitutes or in any manner that makes them palatable

In one case of high ileo-jejunitis where operation was contra

indicated a gain of 50 pounds of weight and a return to fair health and strength followed a conscientious forced attempt at superalimentation with protein foods and amino acid commercial preparations

Foods Allowed in Diarrhea

Milk At least a pint a day Milk need not be boiled Cultured milks may be used acidophilus buttermilk etc Mellin's food or malted milk may be added to milk *Note* Most persons tolerate milk very well However milk may cause diarrhea in those few persons who are allergic to it in such instances the milk should be omitted

Eggs Two or three daily Use in any form except raw or soft boiled

Cheese Any mild cheese may be used cottage pot or sour cream cheese gruyere swiss etc Small portions of sour cream are permissible

Cereals All highly milled grains that are well cooked farina cream of wheat Wheatina cornmeal white rice Ralston etc *Note* When using ready to serve cereals check advertising and reject all cereals containing bran Safe ready to serve cereals are Cerevin corn flakes grapenut flakes pabulum puffed rice puffed wheat Spaghetti noodles and macaroni in moderation

Meats All lean meats boiled baked or broiled ground lean steak roast beef steak liver of all kinds veal lamb smoked ham chicken squabs turkey

Fish All white fish boiled baked or broiled halibut cod flounder sea bass etc shell fish oysters and clams

Bread White bread (not too fresh) melba toast swieback rolls plain sweet breads like brioche also crackers made of white flour

Butter In moderation Thin sweet cream if well tolerated

Fruits With the exception of orange juice and ripe bananas all fruits must be cooked or sieved Use apple sauce pears peaches prune apricots etc

Vegetables Use tomato juice Sweet or white potatoes cooked any way but fried Carrots green pea string beans onions spinach beet turnips tomatoes should be cooked and pressed through a sieve In milder cases cooked chopped spinach and beet tops asparagus tips and fresh tender lettuce may be used Canned infant foods are very satisfactory for use

Desserts Custards Bavarian cream blanc mange bread rice and

tapioca puddings fruit whip gelatin jellies plain sponge and angel cake plain cookies Ices and ice cream are not desirable but may be used in moderation in mild cases

Miscellaneous Strained jams and preserves may be used in limited amounts grape pear apricot and pineapple juices may be used in small portion Juices of all mild cooked fruits may be used with added Dextrin Maltose (not lactose which is laxative) Hard candies are to be encouraged

A certain amount of seasoning is allowable that is salt and pepper in moderation except during steroid therapy

Foods to Avoid During Diarrhea

1 Avoid all raw fruits and vegetables except strained orange juice in small amounts and ripe bananas All other fruits should be stewed

2 Avoid bran in (a) coarse breads (pumpernickel whole wheat bread muffins health breads etc) (b) coarse cracker (whole wheat rye crisp swedish wafers etc) (c) coarse cereal (oatmeal brown rice barley hominy pottijohn etc) Dry cereals are allowed

3 Avoid any gas forming food such as cabbage corn kohlrabi broccoli pickles and relishes of all kinds also skins of baked apples and potatoe Eat no beans peas or lentil except in pureed form

4 Avoid nuts raisins coconuts figs dates etc even if used in small amounts in puddings or cookies

5 Avoid heavy fat foods gravies sausages pastries doughnuts fried meats and fish

6 All condiments especially pepper mustard horseradish vinegar etc are best avoided Therefore do not use any highly seasoned and spiced foods such as smoked meats and fish frankfurters most canned meats and fish salt fish olives etc

7 Avoid fish high in fat—salmon shad etc and shellfish shrimp lobster and crab

8 Avoid all grossly sweet foods preserves most candies all rich cakes with icings and fillings

9 Care must be taken not to use certain foods which are laxative e.g. large amount of lemon grapefruit or orange juice raw vegetable juices long iced drinks and many cups of too hot drinks as well as melons grapes plums molasses raw or soft boiled eggs

Following is the diet suggested for diarrheal diseases

SAMPLE MENU

8 00 a m *Breakfast*

Orange or tomato juice $\frac{1}{4}$ cup (dilute with water if preferred) Cereal with milk and sugar Bread (white) 2 slices (toasted) with butter Egg (1 or 2) boiled hard poached stirred or scrambled Milk cocoa or weak tea (1 cup)

10 30 a m

Hard boiled egg and cracker and milk cocoa or weak tea and cracker

1 00 p m *Lunch or Supper*

Choice of soup strained dried bean or split pea soup or cream soup (made with strained vegetables) or broth and any other strained soup

Choice of main dish Eggs or macaroni and cheese or portion of liver meat or fish

Serving of potatoes rice or noodles Bread (white) 2 slice with butter

Dessert Strained cooked fruit plain cake or custard

3 30 p m

Banana or $\frac{1}{4}$ cup orange or tomato juice (see 10 30 a m)

6 30 p m *Dinner*

Choice of soup

Choice of main dish Lean beef (boil broil or roast) chicken turkey or fish Portion of strained cooked vegetable Portion of potato rice or spaghetti Bread or roll with butter or jelly

Dessert Jello corn tarch pudding or apple sauce Milk cocoa or weak tea

9 30 p m

Milk soft drinks may be taken in small quantities if not too cold and most of fizz is expelled (or see 10 30 a m and 3 30 p m)

Ambulation

Since most cases of regional ileitis are afebrile patients may be allowed some physical activity They are best treated as ambulant cases because the long course of the disease would make persistent insistence upon bed rest a psychic and mental handicap Most of the patients suffering from ileitis are not strong enough to work or attend higher educational schools or colleges but they are happier up and about and would probably gain little from prolonged bed rest Psychologically these patients are better when actively employed and busy invalidism or semi invalidism should thus be avoided Adolescents should be encouraged to read and continue their education even when confined to home The acute cases and those with a febrile course should have bed rest during the active phase thereafter early ambulation is advisable to preserve muscle tone (Femoral phlebitis and pulmonary embolism have not been noted in any cases in this series)

Various Medications

In dehydration particularly with diffuse draining fistula water and electrolyte replacement is best attained by the use of parenteral intravenous therapy. Saline solution Ringer's solution 5 per cent glucose in water or in saline are indicated in amounts of 1500 cc per day or 100 to 150 gram of protein daily. Blood plasma and occasional transfusions of 500 cc are indicated for protein replacement and in instances of advanced anemia.

In chronic ileitis vitamin replacement is strongly indicated. Concentrates of vitamin B complex reinforced by thiamin 10 or 20 milligrams per day may be administered orally although the absorption in the face of diarrhea may be problematic. In all cases intramuscular injection of crude liver extract and of vitamin B complex 2 cc of each should be given into the buttock every other day. Vitamin B₁₂ in doses of 50 to 100 micrograms should be added in cases of severe anemia as well as iron by mouth. It is rare that the other vitamins are indicated there is no material deficit of vitamin A or carotene nor of ascorbic acid nor of vitamin D in instances of ileitis since the diarrhea is rarely so profound as to create such vitamin deficiencies except after extensive and repeated surgical resection or short-circuiting procedures. Synthetic vitamin K is indicated however in all instances of hemorrhage from the bowel wall even though the prothrombin time is well within the normal range. Five to fifty milligrams of synthetic vitamin K daily intramuscularly or by mouth should as an ulcerative colitis control the hemorrhagic manifestations.

The insoluble sulfonamides are indicated in regional ileitis even though the therapeutic result has not been convincingly demonstrated. Whether the disease is bacterial in origin or nature has not been demonstrated. But the bacterial contamination of the intestinal ulcerations and some of the suppurative complications call for antibiotics that would tend to sterilize the bacterial content of the intestinal lumen. Some efficacy of the sulfonamides in controlling the symptoms and progression of the disease seem suggested in studies of the use of sulfazoxidine and sulfathalidine (Crohn) in ileitis though convincing proof is lacking and these drugs in the largest percentage of case fail to accomplish any striking therapeutic result. Sulfazoxidine (succinyl-sulfathiazole) in doses of 0.25 gram per kilogram of weight is frequently employed the usual method is an initial dose of approximately 20 to 36 half gram

tablets (10 18 grams) followed by dosage of 5 to 9 tablets four times daily by oral administration Sulfathalidine (phthalylsulfathiazole) 0.1 gram per kilogram of weight usually 3 to 6 half gram tablet daily are equally efficient

Both of these drugs are bland and relatively free of untoward results Agranulocytosis has not been observed in this series nor has hepatitis been seen except in one instance

Penicillin has no apparent specific effect on ileitis though it is useful in controlling the suppurative complications when walled off perforation does occur As a preoperative and postoperative antibiotic form of therapy penicillin is in great favor with most surgeons Streptomycin too when given intramuscularly 2 grams daily in divided six hour doses and one gram orally coincidentally may sterilize the intestinal tract and produce a sterile culture of the feces It is questionable however whether streptomycin has any clear indications for its use in the chronic protracted form of ileitis

Many of the broad spectrum antibiotics are useful in cases of regional ileitis particularly in the presence of suppurative complications Aureomycin and terramycin because of their side effect in suppressing the normal bacterial flora of the intestinal tract are to my mind contraindicated Chloromycetin is very useful as well as achromycin in 250 to 500 milligram dosage three times daily the newer Mysteclin has a wide range of anti bacterial action without unduly disturbing the intestinal flora and tends to combat the overgrowth of staphylococci and monilia in the feces

As regards steroid therapy the enthusiasm in the prompt sometimes spectacular effect of the steroids as employed in ulcerative colitis cannot be transferred in an equal degree to the treatment of regional ileitis Occasional early reports are beginning to appear in the literature demonstrating favorable effects of ACTH and the cortisones in enteritis but it is still too early to draw conclusions (Gray et al.²) The steroids—hydrocortone cortisone or prednisone—are best given by mouth in dosage up to 15 to 30 milligrams daily Their effect is to improve appetite and well being and reduce fever they have little effect on the diarrheal manifestations An abdominal mass with fistulous intercommunications and skip lesion is not likely to be cured by the steroids but their tendency to throw the patient into a remission of his active symptoms is valuable In higher ileo jejunitis large or massive doses of steroids by mouth (hydrocortone) or ACTH by injection

(Acthar Gel or Cortrophin Zinc) have a decidedly beneficial effect and encourage or encompass such healing as is only possible in the upper segments of the involved small intestine. The Cushing syndrome occurs rarely, intestinal perforation never (Saver Brown and Derrington Stanley Rosenberg and Cleroux).

Radiation therapy has been rather extensively employed; it was originally invoked by Eggers for the control of cases of intestinal granulomas and has been recommended and used by many writers in the literature. Our own experience with radiotherapy in ileitis has been very disappointing though it has been limited to few cases. We have observed the use of extensive radiotherapy in 18 cases, the radiation therapy having been previously employed by clinicians in attempts to control the disease and its complications. Those cases that we have seen have all been failures. If there have been successes in the use of radiotherapy in ileitis they were not apparent in this series under study nor when employed by us as an initial form of therapy. Bopp, Barger and Dixon reported in 1930 the findings of the Mayo Clinic in 50 patients treated by roentgen therapy. In 20 of 43 patients so treated the results were very favorable; the patients became symptom free and were able to return to their former occupations. Fourteen others were improved, 7 were not helped and 2 had died.

In instances of intestinal obstruction the Miller Abbott Harris or Cantor tube is beneficially employed and by decompressing the intestinal lumen produces amelioration of the obstructive phenomena.

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di case which represents healing with scarring and constrictions of the lumen of the bowel. Occasional partial obstruction suggests the lighting up of a previously quiescent lesion here the edema of the bowel wall causes constriction. Localized short circuiting procedures are clearly indicated since decompression of the dilated segment of the proximal bowel is usually protracted cumbersome and only temporarily satisfactory.

6 *Recurrent Ileitis* While most recurrences lend themselves to medical conservative therapy a persistent active recurrence with renewed fistulous tracts hemorrhage or obstruction necessitates a new surgical approach.

7 *Perforation* Free perforation with peritonitis is rare exceedingly so walled off perforations are common. When this occurs with sealed off abscess formation the purulent cavity must be drained at least and the original disease attacked if such can be accomplished without inviting generalized intraperitoneal infection.

Contraindications for Surgical Intervention

1 Diffuse ileitis or ileo jejunitis with involvement of so extensive an area that the sacrifice of the diseased segments would endanger nutrition and invite electrolyte imbalance.

2 Cases of so-called mucosal type in which the lesion instead of remaining stationary shows a progressive tendency to extend orally and invade new proximal segments of the ileum and jejunum.

3 Acute ileitis knowingly to enter the abdomen in the presence of an acute febrile rigid abdomen is to invite disaster and to chance a high mortality rate.

4 Cases of combined ileo-colitis in which both ileum and some segment of the colon are synchronously involved. While surgical intervention is eventually usually a necessity in this complicated form of two combined disease surgical interference should be undertaken only after long and serious thought has been given to the type of procedure to be followed.

The Timing of the Surgical Attack

The increasing consciousness of the high percentage of recurrences after operation has led to much pessimism regarding the surgical end result. The pendulum has of late swung far to the right probably too much so as will be seen shortly in a review of the end results of our

Chapter 12 Indications for Surgical Intervention in Regional Ileitis

OPERATIVE INTERFERENCE is indicated in regional ileitis under certain given conditions.

1 *The chronic localized form of the disease* usually involving the terminal segment of the small bowel which over a long period of time remains static and shows no tendency to spread. A mass is usually palpable in the lower right quadrant of the abdomen. internal fistulous tracts are demonstrable on the roentgen films. fever secondary anemia exist. The mass itself constitutes an indication for operation since it means many loops involved with intercommunicating fistulous tracts such masses rarely heal spontaneously.

2 *Fistulas to the abdominal wall*. These fistulas originate in a diseased segment of bowel indicating persistent and active disease at the base of the fistula and do not heal without some surgical procedure that removes or short circuits the basic lesion.

3 *Perirectal Fistulas*. These fistulas precede accompany or follow active suppurative disease higher up. They do not heal spontaneously but require a surgical attack upon the original focus in the intestine above. Operation upon such perirectal fistulas without first attacking the original focus is fraught with disappointment and much discomfort and invalidism to the patient. The loss of a tonic rectal sphincter leaving a pitulous anus without control in the presence of diarrhea constitutes a most disastrous situation.

4 *Hemorrhage* occurred in 25 instances either as an initial or as a late complication of the disease. Gross bleeding occurs particularly in the postoperative cases with manifest recurrence proximal to the anastomosis. The hemorrhage may take the usual form of melaena but hematemesis is not uncommon. While acute hemorrhage may and usually does subside spontaneously persistent bleeding constitutes an indication for surgical intervention.

5 *Intestinal Obstruction*. Usually a late manifestation of the

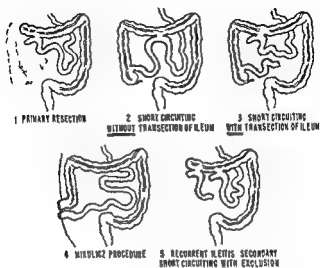


FIG 58a Types of operative procedure

fortune. In most instances the failure to transect the ileum above the upper pathologic limit of disease is accompanied by persistence of symptoms; now a simple transection of the ileum constitutes a curative procedure.^{1, 2}

The type of anastomosis of ileum to colon varies with the individual surgeon. We prefer the side to side method of anastomosis; some surgeons carry out end to side ileocolostomy, thus avoiding a blind loop. The blind loop in the experience of our surgeons rarely gives trouble, but has been known to create severe secondary anemias, to be the source of late gross hemorrhage and occasionally to cause obstruction or proximal dilatation. The side to side anastomosis can be accomplished with greater facility and with less risk of leakage and is most satisfactory.

own more extended series of operated cases. Perhaps the fault lay in the timing of the surgical procedure. Some authors including ourselves thought that radical intervention was indicated as soon as the diagnosis was established. The disappointing late returns created a warrantable atmosphere of caution. Perhaps if the surgical approach were better timed the end results would be more favorable. If operation were delayed until the inflammatory process cooled off and healing resolution were begun the resection or short circuiting would be more successful because among other factors the upper limit of the disease would be more easily recognized at the time of operation. On the other hand too much marching time and procrastination may prolong the debilitating aspects of the disease and leave the patient in an atmosphere of suspense and doubt emphasizing the psychic aspects of the illness.

The best time to operate is when medical conservative treatment antibiotics steroids and rest have been exhausted without avail and after due process of care. This is probably during the second or third year of the illness (see table 13) the follow up of such cases shows the greatest percentage of surgical cures over a long period of time.

Type of Operative Procedures

To a large extent both in this country and throughout the world according to the literature a short circuiting procedure usually in the form of an ileo transverse colostomy with transection of the ileum is the procedure of choice. Certainly it is in our institution the Mount Sinai Hospital where resections are rarely performed. On the other hand primary resection holds promise in the hands of many schools of merit and experience and has many enthusiastic followers. The palliative short circuiting procedure can be accomplished with practically no operative mortality.¹²⁴ Primary resection previously was accompanied by an operative mortality of 12 to 15 per cent but has now according to Van Patter et al. at the Mayo Clinic been reduced to 2.3 per cent. The recurrence rate after either procedure is material but favors the short circuiting operation which is associated with a definitely lower rate of recurrent disease. Since the operative risk is lesser or nil for the short circuiting procedure and the rate of recurrence is less it seems difficult to justify resection as the operation of choice.

In any event transection of the ileum high above the lesion at least 12 to 18 inches is mandatory although even that primary essential maxim is not universally accepted much to our surprise and discom-

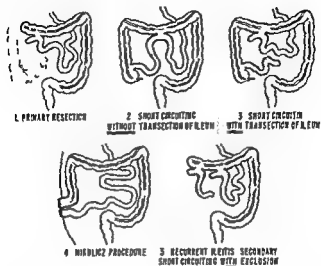


FIG. 58a. Types of operative procedure

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Chapter 13 Surgical Treatment of Chronic Regional Ileitis Historical Survey

THE SURGICAL RELIEF of regional ileitis is indeed a complicated and changing picture. It is very interesting to follow chronologically the trends of opinion over the last 25 years and to note the various schools of thought and procedure. The subject is apparently still in a state of flux as is natural when methods change, procedures differ, judgments do not agree and the follow up period is all too short.

In general one may note historically certain salient or outstanding surgical procedures in the passing years of experience.

- 1 Resection in one stage was the initial procedure of choice
- 2 The gradual evolution of a two stage procedure (short circuiting followed subsequently by resection of the original lesion)
- 3 Adoption of a single stage operation namely ileo transverse colostomy with transection of the ileum as a sufficient procedure to induce cure
- 4 Preference for primary resection by the Lahey Clinic
- 5 Advocacy of a two stage operation by the group at the Mayo Clinic
- 6 Growing realization of the increasing incidence of recurrences following all types of surgical interference

These six stages are described in detail below.

The initial surgical historical procedure at Mount Sinai Hospital practiced by A. A. Berg was primary resection carried out on the first 14 cases of terminal ileitis; this series was increased to 32 instances of resection by Berg in 1936. Correspondingly most of the early cases in the literature concerned themselves only with primary resections of the terminal ileum. In 1936 Koster reviewing 100 operated cases from the literature found resection almost universally carried out as the procedure of choice. In 1939 Ravdin and Johnston reviewing the surgical literature found 290 instances of primary resection against only 88 instances of short-circuiting procedures.

By 1933 we had the suggestion made independently by Clute and by Homans and Hays of ileo transverse colostomy that is short-circuiting of the lesion as a sufficient procedure rather than resection. Unfortunately neither contribution mentioned whether transection of the ileum proximal to the lesion had been performed. Even before this date Estes and Halm had warned against such a procedure; they demonstrated in 2 human cases and by animal experimentation that huge dilatation of the sidetracked and excluded loop of ileum could and did occur. This point of view however was subsequently contradicted by the studies of Ginzburg Colp and Sussman. By surgical experience substantiated by careful roentgenologic studies these latter authors proved that a short circuiting procedure with transection of the ileum was a safe and satisfactory procedure that involved no complication from the excluded loop of ileum.

By 1934 some of the members of the Mayo group (Clark and Dixon) were already experimenting with short circuiting procedures having utilized such a plan in 5 cases out of 13 operables. Again transection of the ileum was not mentioned. In 1939 Clark and Dixon suggested for the early stages of the disease a simple short circuiting procedure with transection of the ileum which carries a low mortality and provides an opportunity for the diseased segment of the bowel to improve by being placed at rest. Subsequent resection of the diseased area was utilized if activity of the original site of the disease continued. If the disease process was far advanced primary resection a radical extirpation of the diseased segment was advocated.

In 1936 Kotter for the first time warned that if a short circuiting procedure is to be performed transection or occlusion of the ileum must be carried out; he still preferred primary resection since he suspected the undesirability of leaving in situ the original focus of infection.

The importance of transecting the ileum above the diseased segment was realized in the following case in this present series.

Case 115 (Serial No 146) Male age 21 years. For 18 months this young man had suffered with diarrhea fever and abdominal cramps. A mass had formed in the right lower abdominal quadrant. He had been operated on at that time and a short-circuiting procedure had been carried out without transection of the ileum. Diarrhea persisted there was a weight loss of 50 pounds edema of the lower extremities was present due to hypoproteinaemia. Clubbing of the fingers and severe secondary anemia (hemoglobin 62 per cent) were evident. At operation a transection of the ileum above the psoas and mesal ileitis was the only procedure employed. This was followed by a regain of the

50 pounds of weight lost and a subsidence of the peripheral edema of the lower extremities. Unfortunately two years later a recurrent ileitis proximal to the old anastomosis was capable of demonstration. A two stage resection of the recurrent ileitis resulted in cure.

The transition of the Mount Sinai group from primary one stage resection to two stage resection and finally to a short circuiting procedure only is interesting to observe. In 1936 though primary resection seemed to be in favor it was noted that both Lewisohn and Colp had 6 cases of short circuiting procedures with good results. Lewisohn later (1938) reported 9 cases of short-circuiting or two stage procedures with only one death. He again strongly emphasized that a lateral anastomosis between upper healthy ileum and the colon without transection of the ileum above the diseased segment is a useless operation since the affected part of the bowel is not put at rest.

In one fatal case a primary ileo transverse colostomy with transection of the ileum had been primarily performed. After a sufficient interval of what was then regarded as the proper sequence the second operation of resection of the primary residual focus of disease was carried out. The resected specimen was now fully healed and cicatrized. Unfortunately the child died postoperatively of pulmonary embolism due to an old rheumatic endocarditis. The tragic death and the evidence that the secondary intestinal resection had been superfluous led to a revision of the views regarding the needs of the secondary resection. Bowen and Day report the postmortem findings in a case of regional ileitis 9 years after symptomatic recovery following ileo colostomy. The ileum previously affected was at the autopsy shown to be fibrosed and sclerotic; the lumen almost obliterated by stenosis and by multiple adhesions. Complete healing of the ileum had been affected by the short circuiting procedure.

In 1939 Ginzburg, Colp and Sussman published 14 cases of short circuiting operations for ileitis, transection of the ileum being regularly carried out. Again they were convinced of the lack of necessity for any subsequent resection; the initial lesion drying up and undergoing atrophy after the short circuiting; fistulae disappearing; abdominal masses resolving. The x ray studies of Sussman convincingly demonstrated no trapping in the excluded loop and good intestinal function through the new stoma.

In 1941 Colp and Ginzburg published a report of ileo colostomy with exclusion as practiced in 22 cases of terminal ileitis with no deaths.

3 of the series showed recurrent symptoms. Four of the cases were reexplored because of persistent diarrhea. In all 4 healing of the original site of infection in the terminal ileum was clearly demonstrable and no further resection was attempted. Six cases had abdominal wall fecal fistulas before operation. After the short circuiting procedure 5 of the fistulae healed and ceased to discharge content. In 1942 Ginzburg and Garlock published 54 cases of ileocolostomy with exclusion with no operative mortality. There were 2 recurrences of the disease in the proximal ileum and 5 cases with persistent clinical symptoms. Contrasted with this were 23 cases of primary resections with 4 deaths and 3 recurrences.

In 1945 a larger group of cases from the Mount Sinai Hospital was published (Garlock and Crohn) covering a 12 year experience with the surgical treatment of chronic regional ileitis. The series comprised 164 cases of enteritis terminalis ileitis and combined ileocolitis most of which had been operated on by various surgeons in that institution (137 cases); the remaining 27 cases had been operated on elsewhere but reported for observation because of persisting symptoms. The inclusion of the latter case which represent failures of previous procedures depresses the statistical value of the total end results of the series but had been included nevertheless in the interests of scientific accuracy. The results may be seen in table 11.

TABLE 11
SURGICAL TREATMENT OF CHRONIC REGIONAL ILEITIS

	Number	Deaths	Recurrences
Ileocolostomy with exclusion	65	0	11 (13.8%)
One stage resection	55	9 (16.3%)	11 (19.8%)
Two stage resection	25	3 (12%)	8 (36%)
Combined ileocolitis	19	2 (10.5%)	3 (17.6%)

By a process of comparison the advantages of the ileocolostomy with exclusion are obvious. The mortality rate was nil the recurrence rate (as of that date) was moderate but yet considerable. The group of cases comprising primary resection was less satisfactory; a considerable mortality rate was apparent nor did there appear to be any compensation for the greater risk since the recurrence rate of resection was even greater than that of the exclusion operation. Here the longer follow up period of the earlier resected cases may well be a factor since recurrences were noted once 11 years and once 12 years after the original operation.

the intervening years having been a period of apparent perfect health Bockus had already noted a recurrence of postoperative ileitis 9 years after apparent good health

The two stage operation consisting of a primary ileo colostomy with transection of the ileum followed some time later by a resection of the primary focus of disease constituted the most distressing group and naturally so because these cases all represent failures of short circuiting procedures the second stage of the operation was forced by the gravity of the persisting symptoms at the original site of disease. Actually they represented failures of the first stage short circuiting procedure. The forced secondary operation was fraught with a moderate mortality (120 per cent) but failed to result in amelioration of symptoms or relief in 36.3 per cent of this smaller series

The Lahey Clinic favored a Mikulicz type of resection for ileitis the diseased ileum and the ascending colon are brought out on the surface of the abdomen exteriorized and resected extraperitoneally. A secondary closure of the enterotomies is later performed. Marshall in 1940 and again in 1943 reported a ten year survey of 55 patients surgically treated. The operative mortality was 55 per cent in a follow up that covered 42 patients of the series there were 5 recurrences or 9.6 per cent

Of this series 35 cases underwent the Mikulicz procedure with but one death a highly commendable record

The group at the Mayo Clinic seem to prefer a two stage operation. In 1937 Pemberton and Brown reported 39 cases of ileitis treated by two stage short-circuiting and resection with 3 deaths. They allowed 3 weeks to 6 months between the first and the second procedure. Transection of the ileum as part of the first operation was always mandatory. In 1938 Dixon reported 40 operative cases the procedures were evenly divided between primary resection two-stage operations and short circuiting alone. Again the gross mortality was low 10 per cent

In 1941 Mayo and Judd reported a full 100 cases 64 of which underwent the two stage operation with a 3 per cent mortality the average length of time between the two stages was 14.4 months. With multiple procedures in the complicated cases Brown and Donald had a higher mortality of 9 per cent for a larger series (178 cases). They suggest surgical removal of the diseased segment of bowel a two-stage procedure is better than a one stage operation

The most disappointing effects are seen when attempts have been made to perform resections of the ileum in continuity with end to end anastomosis of the small bowel. Procedures such as this one are insufficient unphysiologic and lead to skepticism (3 such cases in the present group). This same criticism does not apply to high jejunal involvement where local resection is eminently successful.

In 1938 Dennis suggested vagotomy as a possible cure for ulcerative colitis or regional enteritis. The idea has never proved to be useful but deserves consideration.

Chapter 14 A Review of Our Own Experience With Operative Procedures for Regional Ileitis

OF OUR SERIES of over 500 cases of regional ileitis 385 were subjected to surgical intervention at our instance or were or had been operated on elsewhere the indications for and the timing of the operation having been set by internists and surgeons at other institutions

The main question of surgical interference revolves about one basic question namely which is the better procedure short circuiting or resection? Which of these two procedures is accompanied by the lower operative mortality rate? Which gives the best results as viewed from late follow up studies? What actually is the true figure for recurrences of the disease after either or both of the attempts to cure or to eradicate the primary seat of the disease?

TABLE 12
TYPES OF OPERATIONS FOR ILEITIS AND END RESULTS

<i>General Total 385 cases</i>			
	<i>Good</i>	<i>Recurrences</i>	<i>Deaths</i>
Short circuiting	232 cases—157 (67.6%)	67 (29%)	8 (3.4%)
Resections	116 — 67 (57.8%)	31 (32.7%)	11 (9.5%)

Lost to follow up 37 cases

Many of the cases in this general group were not our responsibility since they had been operated on elsewhere. This over all series might well have been loaded with the failures of others since our office and those of large institutions all become repositories of disappointed failures. We therefore separated our own series of cases i.e. patient in whom the original diagnosis had been established by ourselves in which we set the indications for and the timing of operation and supervised the postoperative course. In addition the personal follow up over succeeding years was more complete and more prolonged. A comparison of our Primary Group—those cases in which we had sole responsibility with those operated on elsewhere should be interesting.

TABLE 13

Primary Group—Follow up Operative Results

		<i>Good Results</i>	<i>Recurrences</i>	<i>Deaths (late)</i>
Short circuiting	125 cases—	86 (68.8%)	34 (27.2%)	5 (4%)
Resection	6	—39 (63%)	17 (27.4%)	6 (9.6%)

Foreign Group—Follow up

		<i>Good Results</i>	<i>Recurrences</i>	<i>Deaths (Operative and later)</i>
Short circuiting	107 cases—	71 (66.3%)	33 (30.8%)	3 (2.9%)
Resect	54	—28 (51.9%)	1 (3.9%)	3 (9.1%)

Total follow up in both series 37 cases

The differences between the two groups is not great

1 As to choice of operation in both groups twice as many short circuiting procedures were carried out as were resections

2 Operative mortality for the primary group was 11 out of 187 or 5.9 per cent. There were 8 additional deaths during the follow up which covered 125 years. The long view mortality for the short circuiting procedure was in the total group (table 11) 3.4 per cent as compared to resections which have a mortality rate of 9.5 per cent.

The immediate operative mortality however is more significant. Of the 12 deaths (in our Primary Group) directly following the surgical undertaking 9 followed resection only 1 a short circuiting procedure. There was 1 accidental death in the operating room.

Obviously the surgical risk attending resection is far greater than that of the by pass operation.

3 The end results again favor the short circuiting procedure 67.7 per cent as against 57.8 per cent for cases which had undergone resection.

4 By the same token the rate of recurrence for the short-circuiting was 29 per cent for resection 32.7 per cent (table 11).

All arguments favor the short circuiting in which the operative mortality is lower, good results higher and the late recurrence rate distinctly lower. Obviously too the recurrence rate is not as often quoted in the literature 35-40-50 or even 60 per cent but by these figures roughly 30 per cent. The 70 per cent of cases quoted as good are free of symptoms except for frequent mild diarrhea, have regained weight, been restored to good nutritional status, do not exhibit anemia and are free of open fistulas. Most if not all of this group have resumed their occupation and domestic activities, many of the women have borne

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Primary Group—those cases in which we had sole responsibility with those operated on elsewhere should be interesting.

children and the men are fertile. Good results are checked by repeated radiographic examinations.

5 The duration of the follow up observation and the timing of recurrences is important.

TABLE 14
FOLLOW UP OF SURGICAL CASES

Short Circuiting—32 cases				Resections (Primary)—116 cases			
Years	Good	Recurrences	Deaths	Years	Good	Recurrences	Deaths
0 1	30	17		0 1	6	5	
2	26	14		2	10	6	
3	12	11		3	11	2	
4	11	5	8	4	5	4	11
5	11	3	Operative	5	3	2	Operative
5 10	11	12	and	5 10	15	11	and
10 15	30	3	Follow up	10 15	10	4	Follow up
15 20	8	2		15 20	5	3	
0 25	1	0		20 25	2	1	
25 30	0	0		25 30	0	0	
157 (67.7%) 67 (29%)				67 (57.8%) 38 (32.8%)			

The follow up covered from 1 to 25 years. It was not complete since 37 cases were lost to follow up. Most of the cases classified as good had been followed for only 5 years but a good proportion over 40 per cent were observed over a period of 5 to 25 years and these maintained their good status with the passing of considerable more time. This statement pertains to both types of operation.

Recurrences

The recurrence rate in our series is roughly 30 per cent. It will be noted from table 13 that most of these recurrences occurred within the first 3 years after operation. Late recurrences are not infrequent and may be observed 5, 15 and even 25 years after the surgical procedure. During this intervening period the patients are well as judged by good nutrition and weight and restoration to living efficiency. A mild diarrhea is not uncommon. Most of these patients are checked at interval by radiographic studies. Time seems to be a most important factor. In 1945 a follow up of a series of 164 cases (Garlock and Crohn) at the Mount Sinai Hospital showed a recurrence rate of 13.8 and 19.5 per cent for exclusion and one stage resection respectively (table 11). By 1951 this rate was revised to a figure of 22.5 per cent and in 1957 to approximately 30 per cent. It is obvious that these later corrections are

when anastomosed to a healthy colon should sooner or later develop a new recurrent disease. If that particular segment of ileum had been left in place it would have remained free of disease for years. Transposed to the colon it develops disease. And this is also true if a second or a third recurrence necessitate the duplication of the operative step. Perhaps only a biochemical explanation will answer this riddle.

It is also difficult to explain the rationale and method of propagation of such recurrence particularly when the operation had been performed by a competent surgeon, one of experience in recognizing the highest possible skip-lesion. In the best of hands where the transection isolating the ileal lesion has been placed high and far distant above any suspiciously involved areas, approximately 30 per cent of recurrences are conceded.

Two possible methods of propagation of the recurrences suggest themselves.

(a) The surgeon is unable to recognize the uppermost skip-lesion and makes his anastomosis too low in the ileum. That this mistake is due to ignorance or inadvertence or inexperience is gainsaid by the fact that recurrence occurs at the hand of the most careful, meticulous and experienced surgeons and are frequently checked by biopsy of the small bowel at the time of operation. Obviously if it is a mistake in judgment it occurs because the mucosal or submucosal infiltration is so minimal as to preclude recognition by palpation or inspection of the wall of the small gut which is utilized for the anastomosis. It seems likely that such skip areas may and do escape the vigilance of even the most adept surgeon. If this is the explanation then the loop of ileum chosen for the anastomosis must be high and far away from any suspected pathologic involvement. Such a high choice invites the danger of nutritional disturbances by sacrificing too much mucosa necessary for food absorption and by inviting the possibility of diarrhea.

(b) The recurrence are due to the persistence of a nidus of residual infection outside the intestinal wall, most likely in the retained and inflamed mesenteric lymph nodes. If such were the case then recurrences should occur with greater frequency after short-circuiting operations than after radical resection—a fact which is contradicted by the table of figures. In the radical excisions of the lesion it is usual to remove the succulent enlarged lymph nodes with the mesentery and with the original lesion, a deep angular resection of the mesentery being performed by most experienced surgeons. However, even with such a radical excision the recurrence rate (32.7 per cent) was higher than with short

Mathieson (1955) 30 per cent at the University of Pennsylvania
 Dyson Hodes and Rhoads (1954) 58 per cent at the Mayo Clinic
 Van Patter et al (1954) 54.5 to 66 per cent

The result of these discouraging late reports was to disparage the successes of surgery in regional ileitis it would seem to us that the pendulum has swung too far to the right and that the over conservative course of delay was often one of unnecessary procrastination and was not warranted by the most recent facts. An operation that can give good results in 70 per cent of the cases and in which the recurrence may take place as late as 5.25 years after the surgical procedure is well worth while as a palliative procedure at least if not necessarily a permanent cure.

Again the question arises as to what constitutes a recurrence. The group at the University of Pennsylvania²⁹ suggest that a distinction exists between clinical and radiological recurrences. The percentage of clinical is far below that of the so called radiological recurrences. The radiologist studying the films of the new terminal ileum is often in doubt concerning the significance of slight irregularity in the mucosal outline of this segment of small bowel just proximal to the anastomosis. Is this a natural irregularity in contour an operative artefact or does this uneven outline signify clinical recurrent disease?

Our own opinion is in agreement with those of the University of Pennsylvania group in irregularity of the new terminal ileum by radiography which has not previously been discerned is significant. But if it is not accompanied by clinical symptoms of recurrent disease the observation and its interpretation must be recorded and weighed. It may well be that the radiological demonstration precedes the onset of true clinical recurrent ileitis.

These recurrences appear almost uniformly in the ileum just proximal to the anastomosis 6 to 8 inches in extent the pathology of the recurrence in the new terminal ileum grossly and histologically resembling that of the initial lesion. Skip lesion above the local recurrence may extend continuously or in an interrupted fashion throughout the remaining ileum and even jejunum. Internal (or external) fistula frequently originate in the involved segment of recurrent ileitis. The recurrence is always in the ileum practically never in the colon even in the absence of any valvular structure the colon exposed for years to recurrent ileitis seem to be immune to the disease. It is difficult to explain why a healthy ileum proved okay by biopsy at the time of operation

permanent ileostomy above the recurrent lesion is the only means of saving life

The very rare involvement of the colon in recurrent ileitis is an interesting negative phenomenon for though there is no equivalent of an ileocecal valve of Baubin at the new anastomosis and though the recurrent ileitis empties unguardedly into the exposed colon the natural immunity of the colonic mucosa to the ileal infection seem to preserve it from involvement by extension This was impressively demonstrated in one particular case an ileitis had been resected 18 years previously the nature of the lesion being little suspected Recurrence of symptoms took place at the subsequent operation 18 years later the recurrent lesion and attached ascending colon were resected en masse the colon was free of disease though probably for most of the long period the recurrent ileitis emptied its content into the large bowel at the anastomosis

The Treatment of Recurrent Ileitis

Fortunately most of the recurrences are mild many of them can be controlled by conservative medical treatment Such therapy consists of drugs that control the frequency of the diarrhea particularly the opiates and Liohin preparations The anemia is treated by the intramuscular injection of crude liver extract vitamin B complex 1 cc of each and B₁₂ 50 to 100 micrograms every second day rest warm climate sunshine at the beach are very helpful An occasional case seem to be helped by radiotherapy sometimes too when emotional strains exist the help of a sympathetic and understanding psychotherapist is welcomed

The insoluble sulfa compound sulfasuxidine or sulfathiazidine are often administered although their value is not proved The newer broad spectrum antibiotics such as achromycin chloromycetin and Mysteclin are very useful in the presence of infection fistula secondary abscesses and fever

The steroids are freely administered for recurrent ileitis as they are for the original disease Here cortisone hydrocortisone as in sprue case 20 milligrams 3 to 4 times daily or Meticorten prednisone or prednisolone 5 milligrams 3 to 4 times daily by mouth The patients seem to do well on the steroids appetite weight and nutrition improve though a true cure of the recurrent disease is rarely demonstrable

An increasing number of recurrences seem to do well they retain only mild clinical symptoms under conservative care and this remains true for long period of follow up years Surgical intervention should

circuiting procedures (29 per cent) If the lymph nodes actually constitute the source of residual infection and reinfection it is necessary to postulate the spread against the normal lymphatic flow which is from the intestine to the lymph nodes rather than the reverse This is contrary to physiologic knowledge though retrograde reinfection and retrograde metastases do occur as in carcinoma Further it has been shown on secondary explorations after short circuiting procedures that when examined the originally inflamed lymph nodes are now diminished in size and show retrogression of the infection

Diagnosis and Treatment of Recurrences

After the operation the patient usually regains weight and strength and appetite hemoglobin values improve fever ceases and diarrhea is absent or only relatively mild The diarrhea after operation may persist for a few weeks or up to six months but usually with time the defecation are reduced to two or three a day without pain or urgency

A recurrence of the disease is marked by a return of fever loss of weight increasing anemia and an exaggeration of the diarrhea The radiographic demonstration of irregularity of the mucosal pattern of the new terminal ileum narrowing of the lumen rigidity and distortion in the 6 to 8 inches of small bowel just proximal to the anastomosis confirm the existence of a recurrence (fig 49) The recurrence is best demonstrated by barium enema the possible involvement of a higher segment of small bowel must be established or excluded by the barium meal study of higher ileum and jejunum Many of these recurrences are exceedingly mild fever is absent loss of weight minimal diarrhea and anemia being the only presenting symptoms Even the diarrhea is undependable a sign of recurrence since postoperative diarrhea even in successful operative cases is not unusual One depends therefore to a large extent upon the radiographic interpretation of the loop proximal to the anastomosis (fig 50) such interpretation is not infallible just as the original radiographic diagnosis of a lesion in the terminal ileum is not always accurate errors of omission and commission being likely to occur

Recurrences with gross intestinal hemorrhage are rare with abdominal wall fistulation or internal fistulas they are somewhat more frequent Recurrences in the colon the rectum and the upper small intestine have been noted fortunately infrequently but they represent a sad picture since little of a further surgical nature can be attempted Sometimes

Secondary recurrences do occur fortunately infrequently. These are usually met when the indications for surgery become mandatory by a third anastomosis usually an ileo sigmoidostomy again with transection of the ileum above the secondary recurrence. These cases too though infrequent occasionally do well the diarrhea following such repeated surgery is not excessive.

A somewhat discouraging report on secondary operations for recurrent ileitis is that of Kiefer at the Lahey Clinic in Boston. Of 42 cases with one or multiple operations 27 were salvaged 10 were disabled 5 died.

The more recent suggestion regarding treatment for extensive diffuse ileitis or ileo jejunitis comes from a Western group. Vagotomy has been experimentally tried for the relief of symptoms and possibly the cure of severe ulcerative colitis. The idea has been extended to cover also the possible very serious forms of ileo jejunitis. Considering that a vagotomy is followed by atony when applied to the stomach it may well be that the putting at rest of the small intestine by the same surgical procedure can be similarly accomplished. Certainly the idea is worth consideration (Dennis et al.).

In cases under steroid therapy it is essential that at the time of operation the steroids should be stepped up rather than diminished. Adrenal atrophy or insufficiency calls for renewed increased dosage before the operative procedure. Electrolyte balance particularly sodium and potassium should be replaced when necessary and during the operation an additional booster dose of soluble cortisone (Cortef) should be administered in the intravenous infusion.

be reserved for those cases only which represent failure under medical regimen and which develop complications such as fever abdominal wall or perirectal fistulas or where the recurrent pathologic process shows an anatomical tendency to extend upward

The surgical procedures for the cure of recurrent ileitis consist of a further short circuiting procedure usually an ileo transverse colostomy distal to the previous anastomosis again with transection of the intervening ileum so as to exclude the newly involved segment. Some surgeons also transect the transverse colon distal to the first anastomosis bringing the proximal cut end out on the abdominal wall as a temporary or mucous colostomy. A second stage procedure is now required to excise the recurrent ileitis and the attached transverse colon. Other surgeons following the principle of short-circuiting merely make the new anastomosis transect the ileum so as to exclude the involved segment and make no attempt further to rectify the recurrent lesion. It is too soon to say which is the preferable surgical approach. It is certainly true that one operation is always better than a two stage procedure provided it suffices to heal the recurrence. The mortality of such operation for recurrent ileitis is exceedingly small and the improvement in well being weight and strength is very satisfactory. Unfortunately too many instances can be cited of extensive and rapidly extending recurrences that defy surgical intervention. Two such cases in this series will demonstrate the almost malignant nature of the rapid and universal involvement of the small bowel by recurrent ileitis.

Case I V (Serial No 229) Male 17 years of age Six months of abdominal pain and diarrhea. Regional ileitis involving the terminal 18-4 inches of the terminal ileum was demonstrated radiographically and at the exploratory operation ileo transverse colostomy with exclusion of the ileum. Recurrent symptoms occurred exactly one year later with rapid downhill course. At exploratory laparotomy thirteen months after the original short circuiting procedure a diffuse ileo jejunitis extending up to the duodenum was demonstrated. No further surgical procedure was attempted.

Case I V (Serial No 110) Female single 29 years of age Eight years of alternating diarrhea and constipation loss of 50 pounds of weight. Eleven months ago resection of terminal 2 feet of ileum (and ascending colon) for terminal or regional ileitis. Six months later because of rapid recurrence of symptoms the patient again underwent surgical exploration. The entire ileum proximal to the anastomosis and the jejunum were the seat of extensive recurrent inflammatory disease. Per stent abdominal wall fecal fistulas resulted after the last and futile exploration. The prognosis was absolutely hopeless.

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Case I W (Serial No 229) Male 17 years of age Six months of abdominal pain and diarrhea Regional ileitis involving the terminal 18 24 inches of the terminal ileum was demonstrated radiographically and at the exploratory operation ileo transverse colostomy with resection of the ileum. Recurrent symptoms occurred exactly one year later with rapid downhill course. At exploratory laparotomy thirteen months after the original hospitalizing procedure a diffuse ileo jejunitis extending up to the duodenum was demonstrated. No further surgical procedure was attempted.

Case I W (Serial No 110) Female single 29 years of age Eight years of alternating diarrhea and constipation loss of 50 pounds of weight Eleven months ago resection of terminal 2 feet of ileum (and ascending colon) for terminal or regional ileitis. Six months later because of rapid recurrence of symptoms the patient again underwent surgical exploration. The entire ileum proximal to the anastomosis and the jejunum were the seat of extensive recurrent inflammatory disease. Persistent abdominal wall fecal fistulas resulted after the last and final exploration. The prognosis was absolutely hopeless.

Warren and Sommer regard acute ileitis as rather common they cite a case reported by Erb and Farmer of a 2½ year old child who at autopsy showed peritoneal effusion marked edema of the ileum and colon closure of the ileo-caecal valve Peyer's patches and generally enlarged mesenteric lymph nodes But of 8 cases of acute ileitis which they themselves observed they regarded 5 as acute exacerbations of a previously existing chronic disease

In the 1949 edition of the monograph we described 16 cases of acute ileitis The sex distribution was about equal the ages varied from 3½ to 37 years at the onset Many of the cases occurred in young children a fact which was confirmed in the current literature Thus the well described case of Erb and Farmer in a 2½ year old child with complete autopsy findings that of Harris in a 5 year old female child Schiff 13½ years of age Warren and Sommers observed that the acute form of ileitis is more severe in young children since the diameter of the bowel is smaller and edema easily produces obstruction

Three of 8 cases reported by Meade occurred in children aged 6 8 and 9 years respectively Megret's case involved a child 3 years of age with successful resection of the involved ileum at the time of exploration Storrs and Hoekelman report acute ileitis in 8 children ranging in all from 3 months to 13 years

Our present or new series (1957) includes 15 cases observed since 1947 Of these 13 were males and 2 females a surprising reversal of our previous figures and seeming to point to a distinct predilection for the male sex The ages varied from 15 to 48 years giving an average age at onset of 28 years almost identical with that of our large series of chronic granulomatous ileitis (27.6 years)

In the present as in the past series the disease is usually restricted to the terminal ileum the area of pathologic involvement extending from 4 to 18 inches in most cases in 2 of the present series at laparotomy the whole ileum was seen to be involved

Skip-lesions as seen in chronic ileitis are not mentioned by the operating surgeons an important observation since it is a clear indication of the fact that the primary seat of the disease is regularly at the terminal ileum the skip-lesion representing a secondary and later extension in time and site The lesion at operation is characteristic the terminal loop of ileum being bright red edematous soggy congested the mesentery thickened the lymph nodes enlarged in some cases not remarked in others In one case an abscess cavity was observed surrounding a per

Chapter 15 Acute Regional Ileitis

IN THE ORIGINAL DESCRIPTION published in 1932 cases of acute regional ileitis were recognized and described. The clinical picture was similar to that of acute appendicitis, namely, generalized abdominal colic pain, tenderness over the right lower quadrant, fever up to 101° or 102° F. The white blood count was elevated. A mass without active abscess formation was fairly constant. At operation the findings were those of a mass of adherent and inflamed loops of ileum, the terminal coil being red, edematous, soft, and brilliantly congested; the mesentery of the gut was thickened and edematous and contained enlarged inflamed mesenteric lymph nodes. Clear or cloudy fluid in small amount was present in the peritoneal cavity. In rare cases an abscess cavity containing thick aqueous but not foul smelling pus was encountered. A general statement was made that some cases were resolved without operative interference, others passed transitionally into the chronic phase of the disease. It was presumed that the acute was but one phase of the chronic disease. The number of cases was too small and the follow up too recent to allow any scientific statements other than a description of the clinical and pathologic picture. Jackman shortly thereafter reported 2 almost identical cases in which the acute picture of ileitis represented only a flare up of the process upon the basis of an old chronic inflammatory lesion in the terminal ileum. Both cases were successfully resected. Erb and Farmer reported 4 cases of acute ileo-colitis in children. Meyer and Ross described 8 cases of regional ileitis, four of which were of the acute type. 3 of these 4 acute cases underwent spontaneous resolution. Rockey described a case of thickening of the terminal ileum, apparently an acute regional ileitis, in a child aged 5 years.

The ample literature that followed from the publications of many surgeons, Clute, Ladd, Harris, Bell and Brunn, and our own present group in this series, amply bore out the facts as set down in the earlier publication. Sufficient time, experience and follow up have now elapsed to warrant a more complete clinical picture, to elaborate upon the life cycle and prognosis of such case. The surgical attack upon acute ileitis has passed through several phases and may now be recapitulated in its present and probably its final formulation.



FIG. 60. Acute ileitis 10 days after onset; temperature 105° F. at onset.

logic curve corresponds almost identically to that seen at operation (fig. 60).

The diagnosis concerns itself practically with the differentiation of acute ileitis from acute appendicitis. The one and only possible clue lies in the presence or absence of diarrhea, since as a rule ileitis is accompanied by diarrhea (14 out of 15 case) and appendicitis by constipation. Unfortunately both symptom complexes afford exceptions to the rule. Ileitis may be accompanied by constipation though rarely (once only in this series) while acute appendicitis may occur with and in the presence of diarrhea. To all intents and purpose, however, appendicitis

foration of the terminal loop of ileum the abscess containing fresh pus. The serosa of the ileum is covered by a serofibrinous exudate free fluid being seen in the peritoneal cavity. The pathologic or histologic findings in acute ileitis are almost identical to those of chronic ileitis. A greater degree of edema is present leukocytic invasion is more prominent. The villi show loss of epithelium and become mere shadows. Very little slough of tissue is to be noted. The serosa is edematous the blood vessels tremendously engorged. The lymph nodes are extremely edematous with marked hyperplasia of the germinal centers (Harris).

The clinical manifestations of acute ileitis show little variation. The onset of symptoms varies from one to 3 days in most cases extending up to 5 weeks. The acute often fulminating onset is characterized by pain in the general abdomen or in the right lower quadrant the pain colicky in nature present in all cases accompanied by fever ranging from 100 to 103 F the curve being constantly elevated and not remitting. Nausea and vomiting are not outstanding symptoms each of them mentioned only in 2 cases an important point in differentiation from acute appendicitis. A mass in the right lower quadrant of the abdomen was clearly palpable in 3 of the cases.

Diarrhea occurred in 14 of the 15 cases constipation is clearly mentioned only once. The diarrhea may be and often is transient may last one day and be followed by normal stools and constipation or may last throughout the acute phase of the disease.

Hematemesis and tarry stools occurred in one case transient intestinal obstruction once. Other unusual manifestations are purpura hemorrhagica (once) erythema nodosum (once) arthralgias (once) these latter unusual signs and symptoms though rare in the acute phase link this abrupt onset with that of the more fully developed clinical picture of chronic ileitis.

The radiographic picture an examination which is usually undertaken some days or weeks before the exploratory laparotomy may demonstrate positively the involvement of the terminal ileum. In all of the 15 cases subjected to roentgen study the localization and the extent of the lesion could be clearly noted. The string sign so characteristic of the fully developed chronic phase of the disease is missing because the cicatrization and the contraction of the lumen of the ileum has not yet had time to develop. The mucosal pattern of the terminal loop of ileum is disturbed the lumen narrowed the proximal gut dilated the contour irregular and shaggy. The extent of involvement as noted by the radio

TABLE 16
FOLLOW UP OF ACUTE ILEITIS, RECENT SERIES (1957)

Analysis—11 cases	Cases
Spontaneous resolution	10
Chronic granulomatous phase	1
Operative—4 cases	
Resection	2
Short-circuiting operation	2
	—
Total	15

Of these 4 operative cases 3 are now well of the 10 cases of spontaneous resolution healing was demonstrated and proved by subsequent negative x-ray examination in 3 of the instances. The follow up of the 12 patients was complete and covered a period of from 2 to 19 years. Only one case was complicated by a perirectal abscess, one by a persistent abdominal wall fistula. There were 2 instances of familial involvement in siblings in one instance 2 brothers in another brother and sister.

The favorable prognosis as regards acute ileitis is borne out by the literature. Of 59 cases 33 underwent spontaneous resolution but of 10 operative cases 5 died as a result of intemperate surgery.

Three questions arise now: (a) Is acute ileitis a distinct entity or is it a part of the picture of chronic regional ileitis? (b) What is the consensus as to the eventual outcome of cases of acute ileitis? (c) What is the proper surgical or medical treatment of acute ileitis?

DISTINCT ENTITY OR PART OF CHRONIC REGIONAL ILEITIS?

Acute ileitis is undoubtedly an individual phase of regional ileitis. It occurs most frequently as an initial phenomenon capable of complete remission in from 25 per cent to approximately 66 per cent of the cases in the remainder advancing to the classic picture of chronic granulomatous ileitis. On the other hand in furtherance of the concept of identity of acute and chronic ileitis acute ileitis may often be regarded as an abrupt exacerbation of the chronic phase of the disease. In many cases a previous history of diarrhea and abdominal pain can be elicited if carefully sought after an occasional bout of temperature a previous rectal operation. Out of this low grade generally unrecognized and unacknowledged course will occur an acute severe episode this exacerbation will again subside and the future course will be identical again with that of chronic regional ileitis (Brown, Lehman, Eliason and

is associated with constipation and vomiting diarrhea has been noted though exceptionally. Endemics of acute gastroenteritis with severe diarrhea may be complicated by a rare incidence of acute suppurative appendicitis (Crohn⁶)

Acute mesenteric lymphadenitis simulates both acute ileitis and acute appendicitis and cannot by any clinical symptoms be identified. Whether acute mesenteric lymphadenitis and acute ileitis are phases of the same disease process if not identical has been suggested and is still an open question (Jackson). Involvement of the terminal ileum in acute mesenteric lymphadenitis has been mentioned (Strombeck) but the transition of acute lymphadenitis to chronic regional ileitis has not been observed.

In this present series the diagnosis was made or confirmed by laparotomy in 9 of the 15 cases or was substantiated at a subsequent operation.

The prognosis in acute ileitis is good in the former series of 16 cases one died due to a brash surgeon's undertaking resection of the lesion in the presence of a fulminating disease. In this present or latter series there were no deaths.

The follow up of the earlier series terminating in 1949 was tabulated as follows:

TABLE 14
FOLLOW UP OF ACUTE ILEITIS (1949)

Nonoperated etc.—4 cases	Cases
Spontaneous resolution	2
Chronic granulomatous phase	1
No follow up	1
Operative—12 cases	
Re section—death	1
Spontaneous resolution—well	2
Chronic granulomatous phase	4
Subsequent host resulting operation	4
Subsequent resection	1
Total	16

Thus it will be noted that only 4 cases of the 16 or 25 per cent went on to spontaneous resolution the remaining cases lapsing into the chronic granulomatous phase of the disease.

The present more recent series demonstrates the subsequent course as seen in the follow up.

TABLE 16
FOLLOW UP OF ACUTE ILEITIS RECENT SERIES (1957)

Van der Vliet—15 cases	Cases
Spontaneous resolution	10
Chronic granulomatous phase	1
Operative—4 cases	4
Resection	3
Short-circuiting—1 case	2
	—
Total	15

Of the 4 operative cases 3 are now well of the 10 cases of spontaneous resolution healing was demonstrated and proved by subsequent negative x ray examinations in 3 of the instances. The follow up of the 1 patient was complete and covered a period of from 2 to 19 years. Only one case was complicated by a perirectal abscess one by a persistent abdominal wall fistula. There were 2 instances of familial involvement in siblings in one instance 2 brothers in another brother and sister.

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Three questions arise now: (a) Is acute ileitis a distinct entity or is it a part of the picture of chronic regional ileitis? (b) What is the conclusion as to the eventual outcome of cases of acute ileitis? (c) What is the proper surgical or medical treatment of acute ileitis?

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Johnson Smithy) Lyall even expresses the view that chronic regional ileitis represents only the end stages of acute ileitis with subsequent fibrosis and cicatrization. The process is primarily an acute one which tends to subside so that the appearance thought by some to indicate a chronic inflammation are really attempts at repair.

EVENTUAL OUTCOME

In our own two combined series (1949 and 1957) 14 out of 31 cases of acute ileitis showed complete resolution as judged by subsidence of all symptoms and in many cases by the change of a positive x ray picture to that of a negative roentgenogram within the course of a few months to a year. The follow up of 2 to 19 years is an assurance that this healing is a positive one since most of these cases have been followed 11 to 19 years without showing signs of a recurrence. If acute ileitis were merely a phase of chronic regional ileitis then the percentage of recurrence in later years should be much higher even though it is difficult to think of a granulomatous disease originating in an acute process.

Meyer and Rosi noted spontaneous resolution in 3 out of 4 cases of acute ileitis. They controlled their observations by radiographic studies in one case involving a child of 7 years of age seven weeks after the exploratory operation the involved ileum appeared roentgenographically negative and free of disease. Another case in an adult female was well one month after the operation radiographic examination revealed a normal terminal ileum. An adult Negro male was observed for 1½ years after exploratory operation for acute ileitis and was and remained radiographically negative for any residual signs of the previous inflammatory focus in the terminal ileum.

In the series of Brown and Donald 7 out of 10 of the acute cases were well 6 of them three or more years after the simple exploratory operation. The series of Warren and Sommers included 15 cases of acceptable acute ileitis 12 of them or 80 per cent regressed 2 progressed and one died. McKinnon reported the spontaneous cure in a case of acute regional ileitis 2½ years after the exploratory operation the patient was well and the radiographic examination which previously had shown involvement of the terminal ileum was now entirely negative.

The subsidence and complete cure of acute ileitis is convincingly shown by most of the cases in the reported literature thus Meyers and Rosi in a follow up of 1 month 7 weeks and 1½ years Brown 2 years

3 years and 4 years. Bigard and Hencke 2 years. Rixford in discussing a paper by Mixer cites a case which had remained well for 8 years after an exploratory operation. In the series reported by Eliason and Johnson 4 cases have remained well for 2 to 6 years. 4 additional cases have remained well for not less than 1 year. One case by Smithy was well 6 years after exploration. The second case showed some radiographic evidence of the disease 6 weeks after exploratory operation but was well with a negative x ray examination 15 months later. In Lehman's series of 7 cases 4 have been free of symptom of the disease from 14 months to 9½ years after the exploratory operation. Kross followed his one case for 7 years of complete restitution. Pugh reports 2 cases of acute ileitis with spontaneous recovery. One case was operated on and acute terminal ileitis observed. 6 months later the case was reoperated on and scarcely any evidence of the original lesion was found. In the second case after an operation for acute ileitis the patient was followed by repeated x ray examination until a completely normal bowel was observed roentgenographically. Probst and Gruenfeld described acute ileitis of terminal ileum with severe hemorrhage enterostomy. Three months later at closing of the fistula the process appeared healed. A small section of the previously involved ileum was removed for biopsy; the microscopic sections revealed only slight round cell infiltration of the subserosa. In a second case only an enterostomy was performed for severe terminal ileitis (15 cm). Two years later the patient was entirely well.

MEDICAL OR SURGICAL TREATMENT

The conservative treatment of acute ileitis consists of avoiding exploratory laparotomy where the best judgment of the observers in terms of patient and surgeon warrants such a course and in the administration of antibiotics sulfathalidin or better the broad spectrum antibiotics such as achromycin erythromycin or streptomycin in large doses usually orally.

The surgical therapy at the time of the exploratory operation may evolve itself into three possible courses of action.

(1) Simple closure of the abdomen. (2) appendectomy alone. (3) closure of abdomen without drainage. (4) a radical procedure (resection or ileo-circumstomy.)

When the preoperative diagnosis can be made with any sense of assurance such as in the presence of diarrhea or a possible previous

Johnson Smithy) Lyall even expresses the view that chronic regional ileitis represents only the end stages of acute ileitis with subsequent fibrosis and cicatrization. The process is primarily an acute one which tends to subside so that the appearance thought by some to indicate a chronic inflammation are really attempts at repair.

EVENTUAL OUTCOME

In our own two combined series (1949 and 1957) 14 out of 31 cases of acute ileitis showed complete resolution as judged by subsidence of all symptoms and in many cases by the change of a positive x ray picture to that of a negative roentgenogram within the course of a few months to a year. The follow up of 2 to 19 years is an assurance that this healing is a positive one since most of these cases have been followed 8 to 19 years without showing signs of a recurrence. If acute ileitis were merely a phase of chronic regional ileitis then the percentage of recurrence in later years should be much higher even though it is difficult to think of a granulomatous disease originating in an acute process.

Meyer and Rosi noted spontaneous resolution in 3 out of 4 cases of acute ileitis. They controlled their observations by radiographic studies in one case involving a child of 7 years of age seven weeks after the exploratory operation the involved ileum appeared roentgenographically negative and free of disease. Another case in an adult female was well one month after the operation radiographic examination revealed a normal terminal ileum. An adult Negro male was observed for 1½ years after exploratory operation for acute ileitis and was and remained radiographically negative for any residual signs of the previous inflammatory focus in the terminal ileum.

In the series of Brown and Donald 7 out of 10 of the acute cases were well 6 of them three or more years after the simple exploratory operation. The series of Warren and Sommers included 15 cases of acceptable acute ileitis 12 of these or 80 per cent regressed 2 progressed and one died. McKinnon reported the spontaneous cure in a case of acute regional ileitis 2½ years after the exploratory operation the patient was well and the radiographic examination which previously had shown involvement of the terminal ileum was now entirely negative.

The subsidence and complete cure of acute ileitis is convincingly shown by most of the cases in the reported literature thus Meyers and Rosi in a follow up of 1 month 7 weeks and 1½ years Brown 2 years

Chapter 16 Ileo-Jejunitis

ILEO-JEJUNITIS may be defined as that form or type of chronic enteritis in which the granulomatous process typical of that disease involves the jejunum either as an extension from the ileum or as an independent lesion limited to all or some of the upper segments of the small bowel.

Very soon after the original publication in 1932 of regional or terminal ileitis it was recognized by Harris Bell and Brunn that the upper ileum and the jejunum could be and were also involved in an almost identical pathologic process. The literature year by year has added new case histories, most of them on the regional form of jejunitis. As early as 1934 Brown, Barry and Weber reported 3 cases of enteritis with the lesion restricted to the jejunum. In 1936 Meyer and Rosi mentioned a case with the inflammatory process localized in the jejunum. In 1937 Pemberton and Brown already noted that 3 of 37 cases of regional enteritis were entirely restricted to localized segments of the jejunum. Lakely and Liss reported in detail 2 cases of high jejunitis, resected ending fatally, and carefully studied at autopsy. These were both localized lesions high in the jejunum causing clinical intestinal obstruction. Ravdin and Johnston in 1939 cited 16 cases of sole involvement of the jejunum in cases culled from the literature.

In 1941 Crohn and Yonisch published an analysis of 17 cases of diffuse ileo-jejunitis with a clinical analysis of the outstanding symptoms and the therapeutic approach to the problem. The differentiation of ileo-jejunitis from sprue was particularly emphasized. Suiman and Wachtel added the distinguishing roentgenographic features in an analysis of 23 cases of granulomatous jejuno-ileitis.

Jejunitis or ileo-jejunitis is not a separate or different disease in all of its major characteristics; it is but a subtype of the more common form of regional ileitis. In its pathology as a granulomatous lesion it is in no major way different from ileitis except in its anatomical distribution. One notes the same clinical characteristics: fever, diarrhea, a mass by palpation, fistulas, rectal complication and anemia. But the degrees of involvement are different; the pathologic process spread over a wider area, the local intensity is less marked in any one segment and fistulas

history of diarrhea fever or a rectal fistula no exploration is justified. In the absence of vomiting or rebound tenderness or of a mass with low fever and a low leukocyte count exploratory operation should be avoided. If operation is undertaken under a false diagnosis simple closure of the abdomen without drainage is advocated.

If however the abdomen is opened and the exploration reveals an acute ileitis should the appendix be removed? There seems little justification for such procedure. Though the practice of appendectomy is common under such circumstances the pathologic report if scrutinized is invariably either negative or else one of chronic inflammation. On the other hand there is really no good evidence to show that appendectomy performed at this time is more prone or conducive to abdominal wall fistula. In the total group of 31 cases appendectomy was performed in most of them yet only 2 abdominal wall fistulas are noted a rather low incidence. Since acute gangrenous appendicitis does occur not infrequently in chronic regional ileitis removal can be advocated as a prophylactic measure.

Is a radical procedure such as resection or a short circuiting operation ever indicated at the time of exploration? The earlier surgeons with experience in this field often advocated radical resection at the time of exploration. The mortality was high however even forbidding.

Since the establishment of the fact that spontaneous healing was not only possible but likely in a large percentage of cases of acute ileitis the consensus favors expectant waiting and noninterference (Koster et al., Brown, Mailer, Eliason and Johnson, Smith, Vaughn, Meyer and Rosi).

That resection or a short circuiting procedure may eventually be come necessary is evident in the follow up of our cases of acute ileitis. In our combined series (1949 and 1957) of 31 cases 9 were subsequently subjected to operation (resection 3 short circuiting 6) most of them with permanent good result although the number of cases is too small to permit tribulated result.

- 2 Involvement of the terminal ileum and upper jejunum by skip lesion—3 cases
- 3 The pathologic process involving upper ileum and lower jejunum continuously—10 cases
- 4 Diffuse ileo jejunitis—40 cases
- 5 Diffuse jejunitis with extension upward to involve duodenum—4 cases and stomach—2 cases
- 6 Localized jejunitis chronic or acute—9 cases

INVOLVEMENT OF THE JEJUNUM BY UPWARD EXTENSION FROM A CHRONOLOGICALLY OLDER PROCESS IN THE ILEUM—2 CASES

Regional ileitis almost always remains in the distal ileum as such and even over the course of years rarely extend upward. However a rare form exists of mucosal or better expressed submucosal ileitis in which the pathologic process advances in an oral direction frequently at a rapid pace to invade the jejunum. We have observed only two instances of this submucosal spread into the jejunum (figs 23 26)

Jejunitis as a complication of ileitis is also seen after unsuccessful surgical procedures in which repeated recurrences take place. Following a resection or a short circuiting of the initial terminal ileitis a recurrence takes place in the new terminal segment of ileum. Another resection is carried out followed by a new recurrence. A third resection may occasionally be attempted any further recurrences may now carry the process up into the jejunum for the sacrifice of involved recurrent ileum may necessitate the resection of a wider area until the whole ileum has been dispensed with and the jejunum is invaded by the malignant extension of the disease process.

INVOLVEMENT OF THE TERMINAL ILEUM AND OF THE UPPER JEJUNUM AS A MASSIVE SKIP LESION—3 CASES

Here one sees an exaggerated skipped area in which the original site of the disease resides in the terminal ileum and by an enormous jump establishes a skip lesion high in the jejunum. These are fortunately rare episodes occurring only in 3 cases in the series but posing a difficult question both in pathology and in therapy. It is most difficult to understand by any view of the pathology of the disease how an extension from an original focus in the terminal ileum can exclude the entire remaining length of the small bowel and reimplant itself in the

and rectal complications are fewer. But the general constitutional disturbance is greater; nutritional absorption is markedly impaired; fever, the enlarged spleen, the clubbing of the fingers indicate the degree of absorption of the toxic products of the disease; skeletal growth is impaired. Hypoproteinemia is a characteristic of the advanced pathologic state.

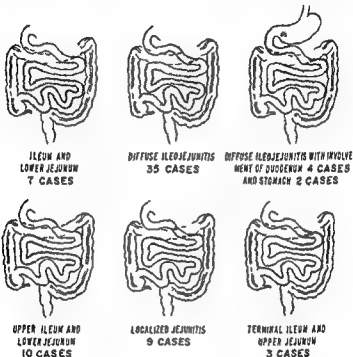


FIG. 61. Anatomical distribution of ileo jejunitis.

The course is low grade, often less severe, a considerable degree of spontaneous healing is possible. The disease is less amenable to surgical therapy than terminal or regional ileitis.

Ileo jejunitis should be considered and studied in its various forms in its anatomic and pathologic variation, as illustrated in the 70 cases of ileo jejunitis which constitute the present series (fig. 61).

1. As an extension upward of an etiologic older process in the ileum—2 cases

Fistulas rarely form the process is typically granulomatous with marked thickening and cobble stone linear erosions of the submucosa and mucosa longitudinally and transversely. Attempts at local excision require massive surgical resection with great risk of life and little assurance of permanent cure. Moreover these localized forms are relatively benign and require only conservative forms of therapy.

DIFFUSE ILEO-JEJUNITIS—40 CASES

This is the most common form seen and constitutes a group of 40 of the total 70 cases under study. Here the whole ileum and the whole or most of the jejunum are involved in a continuous process. Occasion

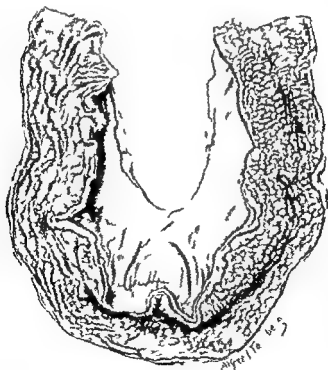


FIG. 63 Pathology in ileum and jejunum

upper jejunum Certainly not by continuity probably not by lymphatic extension Can one contemplate the hypothesis suggested in the German literature³¹³ that originally all of the bowel had been infected and that the disease resolved itself everywhere except at those extremities of the small intestine? Peculiarly these cases lend themselves to surgical therapy namely a local excision of the upper skip lesion in the jejunum and a short circuiting of the distal lesion in the ileum

THE PATHOLOGIC PROCESS INVOLVING UPPER ILEUM AND LOWER JEJUNUM AS A CONTINUOUS PROCESS—10 CASES

This is a not uncommon type of the disease observation of a long period has demonstrated that the process further extends neither upward nor distally but remains static over the course of the years



FIG 6? Lower jejunum upper ileum in old Onst with gross hemorrhage melaena diarrhea and continuous fever

jejunum and the whole ileum being the seat of one continuous process of disease

Chronologically it is impossible to determine which segment is the primary seat of the disease. In practically all of this group the disease had universally involved the whole of the small bowel when first recognized so that it was impossible to state whether the initial process was in the upper jejunum or in the lower ileum. Presumably in this severer type the whole small bowel is simultaneously involved.

Barbour and Stokes in 1936 described a case which at autopsy was shown to have 13 areas of alternate thickening and thinning of the entire small intestine from pylorus to the ileo cecal valve. Halloway's Case 5 showed definite involvement of the third part of the duodenum as well as the terminal ileum and intermediate segments. Rees has described the case of a 30 year old Negress who at operation presented the picture of multiple intestinal obstructions at three points in the upper jejunum due to segmental jejunitis. resection en masse was surgically successful.

DIFFUSE JEJUNITIS WITH EXTENSION UPWARD TO INVOLVE DUODENUM—4 CASES AND STOMACH—2 CASES

These cases occurred all in adults. In all of these six cases the process occupied anatomically the upper jejunum with extension into the 4th, 3rd and even 2nd portions of the duodenum and in two cases with isolated lesions in the antrum of the stomach. the ileum was not incriminated in any of these six cases.

LOCALIZED JEJUNITIS CHRONIC OR ACUTE—9 CASES

The acute case have been described in the literature. one of our cases was acute well defined at exploratory laparotomy. this case went on to spontaneous resolution. The other 5 cases were chronic with localized involvement of a segment of the jejunum clearly demarcated by x ray and restricted to from a few inches (6—8) to 1 to 2 feet of disease. Fistulas and perforation have not been encountered. This type again represents a relatively benign example of the disease.

In 3 of the cases isolated areas of jejunum solely were the seat of the disease. one was 4 inches, one 2 feet and one 4 feet from the fossa of Treitz. a small isolated segment of jejunum 6 to 8 inches in length being the seat of the pathologic process.

Instances of isolated jejunitis have been published by Johnson by

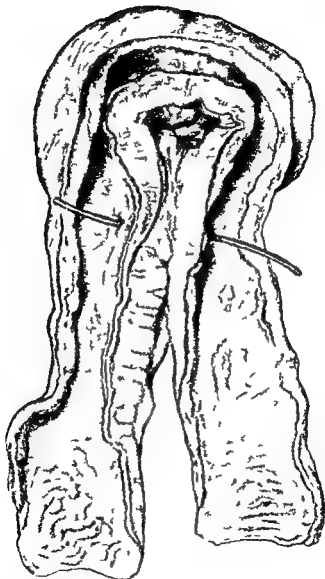


FIG 64 Pathologic lesion involving lower jejunum 6 tula between 1) ps of small intestine

ally in the uppermost jejunum the process is interrupted by the appearance of skip lesions separated by areas of normal mucosa the lower

and Wright as seen at autopsy in 2 cases at Bellevue Hospital. The more recent German literature describes isolated case and cases seemingly occurring as an endemic of extremely grave severity. Wigand noted 37 cases of necrotic jejunitis of which 27 died; the average age of the patients was 55 years; the symptoms were acute, often fulminating and characterized by high fever and intense prostration. Fick and Wolken described (in 1949) 18 cases of necrotic jejunitis from Hamburg, Germany; 16 of the 18 cases died within 7 days; 2 were reportedly saved by early resection. The onset was acute with unusually severe and violent abdominal pain, nausea and vomiting and circulatory collapse. If the patient survives the process resolves itself into the usual form of chronic enteritis.

The whole subject of jejunitis acuta has been summarized in the *Acta Chirurgica Scandinavica* by Johan Hertzberg in 1954. During the last war a large number of cases of the disease were reported in Norway and in Germany. Hausen and his collaborator mention 364 cases of enteritis necroticans in Lubeck in 1946-1947.

Whether acute phlegmonous or necrotic jejunitis in any way related to isolated localized jejunitis as we set it is questionable. Our cases of acute ileitis or acute jejunitis do not die; many of them, if they do not resolve immediately, lapse into the chronic granulomatous form of the disease, whether in ileum or jejunum. It may well be that the European type of acute necrotic jejunitis is entirely unrelated.

Etiology

In this series of 70 cases, 28 were female and 47 were males, indicating a preponderance of male involvement of almost 2 to 1. It is possible that the series is too small to warrant a scientifically accurate conclusion, but throughout the series the major involvement of males is a striking characteristic. (In regional ileitis the proportion of males to females is 5 to 4.) Sussman and Wachtel found a similar incidence of 3 males to 1 female in ileo-jejunitis.

The main brunt of the disease seems to fall in the second decade of life; the third and the fourth decades together contributing an almost equal number. After the age of 40 only a rare exceptional case is seen. The extreme youth of most of these cases of ileo-jejunitis is a striking fact. In the series of 23 cases of granulomatous jejuno-ileitis published by Sussman and Wachtel the average age incidence was 27.0 years, the range varying from 9 years to 65 years of age.

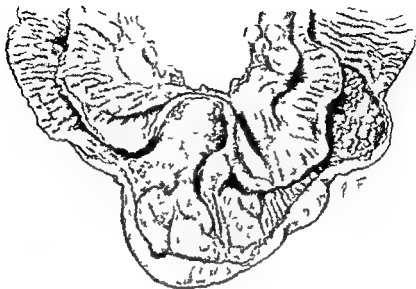


FIG 63 Localized jejunitis occupying uppermost area of jejunum After
nate constriction and dilatation mesenteric lymph n des Characteristic cobble
stone appearance identical with that seen in the terminal form of ileitis

Brewster by Gendel and Beaver by Koemig and by Lyons and Garlock James published 3 cases of regional jejunitis of unusual interest In one case the whole jejunum from duodenum to ileum was involved An anastomosis was made between the stomach and the upper ileum in order to short circuit the lesion In a second case the terminal duodenum and 18 inches of proximal jejunum showed thickened and beefy walls here gastro jejunostomy was performed In the third case 2½ feet of the proximal jejunum showed on exploration chronic inflammatory change again gastro-jejunostomy was performed Cases of primary regional enteritis involving the jejunum following trauma were reported by Browne and McHardy and by Spellberg and Gray

Kazmann and Barnett in 1951 published a case of acute localized upper jejunitis the diagnosis confirmed at exploratory laparotomy No resection was attempted the patient made a rapid recovery from the surgical procedure and remained asymptomatic for two subsequent years of observation

An acute phlegmonous or necrotizing type was described by Clark

thickening edema and congestion. Since much healing is capable in the upper small bowel areas of contraction moderate or extreme may appear with intervening dilated and distended loop of intermediate bowel (fig. 65). Where two or more areas of constriction occur the intermediate bowel may be much distended. This over distended loop may give rise to necrosis of the bowel wall with abscess formation. Or a perijejunal abscess may form in the thickened and inflamed mesentery, the abscess being walled off and localized. When such an abscess forms it may become adherent to the abdominal wall at the site of the scar of a previous incision and discharge its contents. Fecal fistulas to the abdominal wall are however rare. The lymph nodes of the mesentery are enlarged and succulent similar to those seen in distal terminal ileitis. Microscopically the process is identical to that of ileitis and of intestinal granulomata in general. Miliary like tubercles consisting of lymphoid and epithelioid mononuclear and plasma cells are common and frequently enclose giant cells presumably of foreign body nature. The lymphoid follicles are hyperplastic with active germinal centers. In their excellent article Gussman and Wachtel describe the pathology as well as the radiologic appearance of the disease as occurring in three stages namely acute subacute and chronic. The acute stage is characterized by edema and thickening of the mucosa and of the adjoined mesentery, the subacute stage by a granular and hypertrophic mucosa containing punched out ulcerations with smooth or irregular edges the ulcer being either longitudinal or transverse to the axis of the bowel early polypoid proliferation and evident lipoleiomas are discernible. The chronic stage is characterized by thickening and fibrous alternating areas of atrophic and hypertrophic mucosa multiple areas of stenosis the area being covered by a shaggy exudate. This description includes the findings at four autopsies and the intestinal biopsies obtained at three of eight exploratory laparotomies and represents an accurate and painstaking study of the pathologic changes in the three various phases of the disease.

Several forms of isolated jejunal ulcers appear in the literature although there is some question as to the identity of such ulcer with the granulomatous forms which are recognized as ileo jejunitis. Richardson in 1922 was responsible for the first American description he cited 2 cases of jejunal ulcer with stricture and perforation. Buckstein gave a good description of primary ulcer of the jejunum. Robinson and Wise in 1940 reviewed the whole literature and culled the large number of

The age incidence in this series is striking and indicates a preponderance of involvement in the earlier decades of life (table 17)

TABLE 17
ILEO JEJUNITIS AGE INCIDENCE

<i>Age at onset in Years</i>	<i>No of Cases</i>
1 10	5
10 20	27
20 30	23
30 40	11
40 50	3
50 60	0
60 70	1

Total 70 cases

No new or significant factors as to the causation of ileo jejunitis are known as distinct from regional ileitis. The same fundamental ignorance as to causation and etiology which covers ileitis applies also negatively to ileo jejunitis. In only one of the 70 cases in the group which forms the basis of this study was physical trauma attributed as a causative factor. Trauma however has exceptionally been recited in the literature (Browne and McHardy, Spellberg and Cray).

Pathology

The pathology of ileo jejunitis differs little from that of regional ileitis. Grossly the small intestine is bluish red in appearance the serosa streaked by inflamed lymphatics. The wall is thickened coarse and firm where long standing healing has taken place the lumen may be contracted and the wall of the gut puckered. When the resected specimen is opened the mucosa is cobble toned in appearance as seen in ileitis cross hatching of longitudinal and transverse ulcerations creating that appearance. The mucosa is thrown up and prominent in places appearing as and even assuming a polypoid excrecent form. True inflammatory polyps occur frequently and can be visualized in the roentgenogram. The ulcers in the mucosa penetrate to the inflamed thickened submucosa these ulcers rarely penetrate more deeply and do not with rare exception form fistulous tract. The whole wall submucosa muscularis and serosa is involved in the granulomatous and cicatricial process as evidenced by

Diarrhea is the most constant symptom occurring in most of the 70 cases in this series constipation is noted 4 times only normal bowel movements prevailing in the remaining instances The diarrhea is never extreme averaging usually 2 to 4 movements per 24 hours The stools are mushy or semisolid mixed with thin mucus occasionally they are watery Pus is never seen gross blood in flecks only exceptionally The guaiac reaction was positive in 10 cases negative in the remainder In fact it is not unusual to have negative guaiac reaction in the feces of proved cases throughout the course of the disease

Abdominal pain is another almost constant symptom having occurred in 56 of the 70 cases in this group The abdominal pains are crampy in nature diffused over the abdomen or more likely to be localized over the left upper quadrant The pain may be mild and associated with the desire to defecate or severe and definitely predefactory in timing With the passage of fluid feces and gas accompanied by an audible gurgling the cramp is allayed When obstructive phenomena are present the abdominal cramps are more or most severe occasionally accompanied by vomiting

Gross hemorrhage occurred once in this present series In a previously studied series it occurred three times as an initial symptom out of 17 observed cases The gross hemorrhage takes the form of melaena (5 cases) though once it was accompanied by a brisk hematemesis The hemorrhage while profuse is never exsanguinating and usually not associated with shock

Symptoms of obstruction are frequent and occurred in 17 of the 70 cases The intestinal obstruction is frequently of low grade relieved by the Harri tube few of the cases being of such severity as to require operation for advanced obstructive phenomena The obstruction is usually inflammatory in nature and is due to edema of the bowel wall possibly accompanied by a perijunal or a mesenteric abscess and subsiding as the inflammatory process recedes Vomiting was noted in 5 cases Browne and McHardy mention obstruction as one of the symptoms in their case of a Negro boy who developed a localized jejunitis following a severe abdominal trauma

Anorexia and weight loss are common manifestations The loss of appetite is spotty and occurs during acute exacerbation of the chronic process at other times appetite may be well maintained

The weight loss may be very severe amounting in some of our

36 cases of solitary ulcers of the small bowel of which 7 were jejunal Dowdle adds a case of multiple primary nonspecific jejunal ulcers with duodenal dilatation the bowel was obstructed not much below the ligament of Treitz with dilatation and thickening of the intestine above the strictured area

Symptomatology

The rare acute forms of ileo jejunitis are characterized by abrupt onset with fever diarrhea and abdominal pain a mass may be palpable in the left upper abdomen a high leukocyte count is common Clark and Wright cite 12 cases from the literature in which the duodenum was involved associated with vomiting

Husebye presented 14 cases of acute phlegmonous jejunitis as seen by x ray in six instances the diagnosis rested essentially on the roentgen appearance of the films seven of the fourteen patients recovered The roentgen findings were characteristic and consisted of (1) reduced diaphragmatic movements on one or both sides (2) scout films which revealed distended loops of gut over the left abdomen (3) erect films which revealed fluid level (4) barium meal procedure which showed the mucosal relief to be roughly jagged with irregular circular folds partly sharp and partly blunt

The classic form of chronic ileo jejunitis or jejunitis is that of a low grade granulomatous inflammatory lesion involving primarily the jejunum either continuous with a similar process in the ileum or else associated with an independent lesion in the distal ileum

The onset is usually gradual and prolonged lasting from six months to fourteen years or more The actual onset is often difficult to estimate since the occasional slight diarrhea mild fever or loss of weight is little noticeable

The outstanding clinical symptoms are (a) low grade fever (b) diarrhea (c) severe abdominal pain (d) gross hemorrhage (e) symptoms of obstruction (f) anorexia (g) loss of weight (h) anemia

Fever was present in 16 of the 70 cases in this series the fever is intermittent in type higher in the later afternoon or evening it may rise to 103° F though usually the range is between 100° and 102° F temperature chills are occasionally noted The fever may be so mild as to be almost imperceptible and may not be accompanied by malaise or prostration The fever may be paroxysmal remaining continuously for several weeks or months or may be interrupted by periods of apyrexia

narrowing with localized dilatation and constricting. Serum calcium was 8.0 and 8.2 milligrams per cent inorganic phosphorus 3.5 and 3.8 milligrams. Vitamin A absorption of 250,000 USP units was only slightly below normal levels. fasting serum carotene almost normal. The patient improved rapidly under high protein diet and amino acid concentrates. The intravenous administration of amino acids did not improve the nitrogen balance or create nitrogen retention in the metabolism studies.

Loss of fat soluble vitamins was especially emphasized in Albright and Stewart's report. The case a woman aged 35 years had undergone 4 successive operations for ileitis and recurrent ileitis including 2 extensive intestinal resections. Protracted severe abdominal cramp and diarrhea resulted in tetany and a state of marked vitamin deficiency. The prothrombin time was found to be only 13 per cent of normal indicating a marked associated vitamin K deficiency. Vitamin C was within normal range. Fat soluble vitamin A was somewhat deficient 8.2 units per 100 cc of serum (normal 10-20 unit) carotenoids somewhat diminished and associated with an xeroderma of the breast and abdomen. Fat soluble steroids particularly the quantity of 17 keto steroids in the urine were practically absent. The tetany responded rapidly to large doses of vitamin D 500,000 USP units daily. The results of treatment in the form of liberal dosage with all of the fat soluble vitamin preparations were clinically dramatic.

An unusually exaggerated degree of hypoproteinemia was noted in a diffuse case of ileo jejunitis by Cistren. At a previous operation an anastomosis between the upper jejunum and the transverse colon had been performed because of a diffuse inflammatory process involving all of the ileum and the lower jejunum. Extreme malnutrition and evidences of hypoproteinemia were soon evident. The total serum proteins fell to 3.1 grams per 100 cc the albumin fraction being 1.1 Gm and the globulin 2 Gm (albumin globulin ratio 0.55). Most observers conclude that the critical level of serum protein being 5.0 Gm per 100 cc edema will invariably result when the blood level falls below that point. Hypoproteinemia occurs 5 times in this series.

Blood changes. The white cell count varies only a little from the normal a very mild leukocytosis up to 8,000 to 10,000 or even 18,000 white blood cells may be noted though most usually the count is within the lower range of normal. Eosinophilia as seen in ulcerative colitis is unusual although it was seen in 5 patients of our previous series up to 14 per cent of eosinophiles being present in the blood smears. A mild

cases to as much as 50 pounds in a stout girl. The average loss of weight in our previous series was 17½ pounds. During the healing phases with remissions of the fever and diarrhea the weight may be rapidly regained. 15, 25 or even 50 pounds may be added during prolonged remissions of the symptoms.

The *nutrition* is usually poor. skin is dry, mucous membranes pallid. An extreme degree of malnutrition with inanition and loss of strength marks the end stages of lethal cases. Retarded growth and retarded sex maturation are commonly observed in the young adolescents who are so frequently affected by the disease at a prepubertal age. With the recovery from the severe phase and with healing of the lesion advancing weight, growth in height and secondary sex maturation may replace the hypogonadism seen in the adolescent years. One of our earlier cases who had remained stunted in growth and devoid of secondary sex characteristics later recovered fully from the diffuse ileo jejunitis from which he had suffered, grew to be a strong well developed man married and was the father of two children.

The menses are rarely skipped in ileitis as they are in severe ulcerative colitis. Several cases of ileo jejunitis have married and borne normal children without detriment to their general health or difficulty and without the induction of a recurrence of the disease process.

Aphthous stomatitis (3 cases), furunculosis, erythema nodosum, epidermolysis bullosa were each seen once. Phlyctenular conjunctivitis was twice seen. occasionally one notes bleeding gums, glossitis as evidence of nicotinamide deficiency and riboflavin deficiency as marked by cheilosis though the latter are extremely rare. Vitamin A deficiencies, night blindness and the bone changes of vitamin D deficiency have not been noted.

Killian and Ingelfinger studied the nutritional problems presented by a patient with extensive ileo jejunitis. A 23 year old boy with a previous history of a loss of 40 pounds of weight was aboard a ship torpedoed during the recent war and was exposed in a life raft for eight days. He was found in a state of extreme malnutrition, emaciated, dehydrated, with pitting edema of the lower extremities. The tongue was smooth, fever up to 102° F., hemoglobin 54 per cent, red blood cell 1,200,000, hematocrit 22 per cent, serum protein was markedly reduced to 4.85 grams per 100 cc., albumin 2.34, globulin 2.51 grams per cent. Clubbing of the fingers was present, the glucose tolerance test showed hypoglycemia with a low tolerance curve. By x-ray examination the lower jejunum and the ileum showed marked irregularities and points of

in a very severe case of ileo jejunitis. The albumin globulin ratio is disturbed approaching a ratio of one but rarely completely reversed.

The urea phosphorous blood chlorides and blood sugar are but slightly if at all lowered. The blood calcium may be materially reduced. 2 of the patients in our present series having shown frank symptoms of tetany.

Gastric analysis showed normal titrable acidity in all cases except one of achylia gastrica.

The physical examination of a case of ileo jejunitis may not be



FIG. 10. Clodding of finger in a case of diffuse ileo jejunitis with involvement of the whole jejunum and the upper ileum. palpable spleen.

secondary anemia was present in 12 out of the 36 cases in this series, the range being usually between 72 and 50 per cent hemoglobin (Sahli). A macrocytic hyperchromic type of anemia occurred once in our previous series with a color index of 1.3. In this series of 36 cases hyperchromic anemia was not observed even though the anemia was at times severe and the intestinal absorption severely compromised as evidenced by hypoproteinemia. The hyperchromic anemia in ileo jejunitis is usually not beneficially influenced by intramuscular injections of crude liver extract, the reticulocyte response attaining a level of only 7 per cent, this in contrast to its more successful therapeutic result in cases of non-tropical sprue.

The occurrence of macrocytic anemia in association with intestinal lesions, particularly intestinal strictures and anastomoses, was amply demonstrated in the literature by Faber, Hale, White, Meulengracht, and by Hurst. Butt and Watkins mention 7 cases of diffuse ileitis with macrocytic anemia, in 6 of which a fecal fistula coexisted. With proper reconstructive surgical intervention the macrocytic type of anemia could be returned to a normal blood picture. They rightly ascribe the hyperchromic anemia to the abnormal interference with absorption and improper utilization of the effective hemopoietic fraction of the diet. Plum and Warburg, in a publication entitled "Hematological changes especially megalocytic anemia in regional ileitis," describe 4 cases under their personal observation in which the blood picture was typical of that of a hyperchromic anemia. The hemoglobin values ranged as low as 20 per cent, red blood cell count as low as 1,410,000 cells, color index 1.12, 1.19, 1.15, 1.05 at the point of greatest severity. In one case the jejunum seemed definitely to be involved. Barker and Hummel similarly quote a case of ileitis with resection and a secondary short-circuiting operation and a consequent hyperchromic anemia.

Sprue, a disease without noticeable organic changes in the intestinal mucosa but with completely deficient intestinal absorption, is often characterized by a hyperchromic or macrocytic type of anemia. Ileo-jejunitis, by contrast, is a disease with extensive organic destruction of wide areas of intestinal mucosa, yet absorption is better maintained in spite of severe and extensive ulceration. A hyperchromic type of anemia is rare.

The erythrocytic sedimentation rate may be somewhat accelerated as seen in 5 patients. The total blood protein of the plasma is appreciably diminished in the more severe cases (5.8 Gm.) reaching a minimum of 4.0, 4.4, and 4.5 grams per 100 cc. in 3 cases and as low as 3.8 grams

stricture and dilatation which are present as obstructive phenomena in ileo-jejunitis are absent in sprue (figs 67 and 68)



FIG. 67 Ileo-jejunitis of the upper ileum and lower jejunum. Resection in continuity at the Mayo Clinic, complete restoration to health.

In ileo-jejunitis marked general clinical improvement may be noted as a result of general hygienic measure and the forceful administration of the steroid but the diffuse string signs throughout the ileum and jejunum are irreversible and remain permanent even though general good health and nutrition have been restored. In cases of diffuse ileo-jejunitis without obstruction observed over a course of years (10-22 year) complete subsidence of symptoms with regain of 50 pounds or

noteworthy. Some of the cases show well maintained nutrition others may give evidence of pallor and extreme malnutrition in the later stages of a deteriorating status. A mass is occasionally present (8 cases) usually in the left upper abdomen corresponding to the inflamed mesentery of the jejunum with the associated granulomatous loops of bowel. Such a mass may often be adherent to the anterior abdominal wall forming a localized abscess that requires incision and drainage. External fistula to the abdominal wall occurred 7 times in this series. Internal fistulas ileum to jejunum or jejunum to jejunum occurred 4 times.

In case of localized subacute intestinal obstruction the whole abdomen may be distended, visible peristalsis was seen when the degree of obstruction became complete and almost always associated with vomiting. The edge of the spleen was distinctly felt 5 times in this series frequently associated with clubbing of the fingers which was noted 13 times in all.

The clubbing of the fingers and occasionally also of the toes is a significant observation and indicates the extreme degree of constitutional alteration invoked by so diffuse an intestinal dysfunction (fig 66). Cooke found clubbing of the fingers to be present in 48 out of 90 cases.⁴

Rectal complications do not occur with the same frequency in regional ileitis. In this series peri rectal abscesses and fistulas occurred 11 times, a vesical fistula was never observed.

Differential Diagnosis

The main point of interest lies in differentiating high ileo jejunitis from sprue and from the secondary vitamin deficiency manifestations. Sprue is characterized by typical frothy and fatty stools, by a severe secondary anemia or by one of hyperchromic type with a high color index. Fever is absent, the stool does not contain blood, gross hemorrhage either as melaena or hematemesis is missing. The sprue case or that of vitamin deficiency reacts well to deep injections of crude liver extract, vitamin B complex and of B₁₂ but particularly now is well controlled by steroid therapy, especially hydrocortone in large doses by oral administration or parenterally. With such therapy the sprue or deficiency case may show a partial or complete reversal of the disturbed mucosal pattern in the small bowel with a restitution to the normal appearance.

The lower or terminal ileum is usually free of disease in sprue in jejunitis and certainly in ileo-jejunitis the distal ileum constitutes a major area of pathologic disturbance. The intermittent areas of con-



FIG. 69 Diffuse ileo jejunitis observed over a course of several years

such as accompany severe ulcerative colitis give roentgenographic changes similar to those of sprue and often to those of mild diffuse jejunitis. They have been described by Snell and Camp, by Mackie and Pound, and by Adlerberg, and Weingarten. Mild puddling, delay in jejunal loops, irregular outline of the upper ileum and lower jejunum, such as occur in sprue and in jejunitis, may be present; there are no manifestations of delayed motility, and no obstructive or polypoid change in the roentgenograms.



FIG. 88 Diffuse jejunitis in a boy of 17 years of age confirmed by exploratory operation. Rapid downhill course.

more in weight has been repeatedly observed. The continual radiographic examinations year after year show the same intermittent string sign occupying ileum and jejunum as seen at the first observation. Evidently permanent scarring and cicatrization of the intestinal wall had persisted in spite of restoration of health and integrity.

The vitamin deficiency states with disturbance of fat metabolism

ileitis must be recognized in the differential diagnosis where more common diseases of febrile nature receive first presumptive consideration. Disease characterized by continuous fever with low leukocyte counts include such syndromes as brucellosis, rheumatic fever, periarteritis nodosa and lupus erythematosus disseminatus. The advent of diarrhea so often overlooked or ignored indicates the possibility if not the likelihood of ileo jejunitis being the true cause of the febrile state (fig. 70).



FIG. 71 Sprue—characteristic segmentation in loop of small bowel

If lipple's Disease

Avery Jones and Paulley called attention to the possible relationship of intestinal granulomatous lipodystrophy and regional ileitis. Intestinal lipodystrophy may simulate ileo jejunitis and requires differentiation from it. This condition is characterized by a sprue-like diarrhea



FIG. 70 Same case as figure 66 two and a half years later. Subsidence of symptoms. Gain of fifty pounds of weight. Absence of stenosis and stricturing.

Hodgkin's disease of the small bowel and diffuse multicentric sarcomatosis of the mesenteric lymph nodes with intestinal involvement are rare diseases which simulate jejunitis. Both of these diseases are extremely malignant; the course is rapid and downhill and perforation and hemorrhage not uncommon (figs. 57 and 58).

Continuous fever of intestinal origin arising in ileo-jejunitis or

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FIG. 71. Spiculate—characteristic segmentation in loops of small bowel.

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examination. In the duodenum the third and fourth portions occasionally also the second portion become thickened and rigid and converted into a semi rigid tube. The periduodenal tissue and the pancreatic capsule may be inflamed and edematous. The cecum is engorged and red dened and the regional lymph nodes are enlarged. The microscopic picture as we have seen it in 2 cases has been compatible with that of granulomatous enteritis namely infiltration with plasma cell and fibroblasts with epithelioid and giant cell formation. Fistulization between the stomach or duodenum and adjacent viscera is unknown as is perforation. The clinical picture is dominated by obstruction.

Almost always the local process in the stomach and duodenum is part of a more diffuse process involving one or more segments of the small bowel. Occasionally the involvement of the duodenum represents an exceedingly high skip-lesion from an original focus in the distal or terminal ileum.

In our present series we can add 4 more cases with involvement of the duodenum and 2 cases with nonspecific gastric lesions. One of these 4 cases of duodenal involvement was acute in nature and was resolved without operation. Radiographic examination a year later showed no evidence of the previous well marked disease. In one case with involvement of the stomach a gastroenterostomy was performed with relief of symptoms. In the second case of gastric and duodenal and jejunal involvement but without obstructions a two year follow up showed persistent symptoms. on re x ray after two years the lesion in the stomach was no longer evident but the remaining lesions were unchanged.

Clinical Symptoms

In the esophagus symptoms are dominated by sub sternal burning pain or heartburn with progressive dysphagia. In the gastric cases Comfort has noted upper abdominal pains made worse by the ingestion of food with nausea vomiting, diarrhea and progressive weight loss. The vomiting and pain are the outstanding features. Gastroscoy has shown diffuse superficial gastritis with multiple areas of surface ulceration. The gastric test meal is not unusual. occult blood in the fractional specimens is usually present.

In duodenal involvement obstruction is the predominant characteristic usually with protracted vomiting and rapid and extensive loss of nutrition and of electrolytes.

and progressive loss of weight and strength associated with rheumatic and serous membrane manifestations. It has been considered to be a collagen or connective tissue disease probably stemming from an underlying fundamental metabolic defect in the function of the intestinal mucosa. A marked elevation of the serum glycoproteins exists with deposits of glycoprotein in characteristic foamy macrophages predominantly in the lamina propria and in the lymph nodes of the intestinal tract and of the body in general as typical granulomata. The diagnosis can be established by a biopsy of the peripheral lymph nodes adenopathy occurring in about 50 per cent of the cases. The disease is amenable to steroid therapy in many instances (Purte and Tesluk).

Primary Jejunal Ulcer

As an isolated phenomenon this entity has occasionally been described in the medical literature. The lesion is usually located in the upper jejunum. In several instances perforation followed trauma with acute peritonitis. Secondary severe anemia of such ulcers is not uncommon (Muehlbauer et al.).

Granulomatous Disease of the Duodenum and Stomach

The increasing frequency with which a non specific pathologic disease of the duodenum and stomach is being recognized particularly as part of the picture of ileo jejunitis calls for special attention. The literature has recently been thoroughly summarized by Richman. Medical reports up to the year 1954 comprise 28 such well documented cases.

In 1939 Shapiro reported 2 cases of regional enteritis involving the terminal duodenum and the proximal jejunum. In the same year Ragnotti described a similar case. In 1946 Menzel and Boying added 2 additional almost identical cases in addition to one reported by Janus. In 1949 Ross described in detail an instance of involvement of the stomach small intestine and colon. In 1950 Comfort et al. added 3 new cases. Eighteen additional cases have since been added to the literature making a total of 28 reported cases of involvement of stomach and duodenum and including one instance of the involvement of the esophagus (Carlisle and Judd, Marten and Carr, Anderson, Mullinger and Bogoch).

In the cases in which the stomach was involved the posterior wall and greater curvature of the stomach were the usual site of the inflammatory process. A mass resembling a small benign tumor may be felt and seen at the operating table and has been seen also by gastroscopic

examination In the duodenum the third and fourth portions occasionally also the second portion become thickened and rigid and converted into a semi rigid tube The periduodenal tissues and the pancreatic capsule may be inflamed and edematous The cecosa is engorged and red dened and the regional lymph nodes are enlarged The microscopic picture as we have seen it in 2 cases has been compatible with that of granulomatous enteritis namely infiltration with plasma cells and fibroblasts with epithelioid and giant cell formations Fistulization between the stomach or duodenum and adjacent viscera is unknown as is perforation The clinical picture is dominated by obstruction

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In duodenal involvement obstruction is the predominant characteristic usually with protracted vomiting and rapid and extensive loss of nutrition and of electrolytes

Radiologic Features

In the single case of esophageal involvement in the literature the distal third of the esophagus proximal to the lesion was somewhat dilated. In the gastric cases the radiologic picture is one of pyloric or post pyloric obstruction without marked dilatation of the body of the stomach. The duodenal bulb may be somewhat deformed though actual involvement of the first part of the duodenum has not been verifiably demonstrated. The second portion of the duodenum may radiologically appear thickened and rigid but involvement of the Papilla of Vater with jaundice has not been described. The third and fourth portion of the duodenum may be converted into a rigid tube with loss of haustral markings and with evidence of obstruction and narrowing proximal dilatation with stasis and with food residue exists. A true string sign may occasionally be observed (fig. 47 page 98).

Diagnosis

The diagnosis of the lesion when present in the esophagus stomach and duodenum usually depends upon the finding of concomitant lesion elsewhere in the small bowel. However in 11 cases in the literature the disease was limited to the stomach and duodenum.

Treatment

The treatment of granulomatous disease of duodenum or stomach is usually surgical. Medical treatment is purely symptomatic. Gastroenterotomy will suffice to relieve the symptoms of obstruction in the duodenum more radical excision of involved segments is both impossible and unnecessary. Again as in terminal ileitis a side tracking procedure is all that is required a transection isolating the diseased portion is not usually performed (Green).

Involvement of the antrum of the stomach particularly when hemorrhage is present calls for subtotal gastric resection. Subsequent postoperative gastro jejunal ulcer has not been reported.

Chapter 17 Malabsorption in Ileitis

by DAVID A. TURNER PH.D.*

THE NUTRITIONAL STATUS of man on an adequate food intake depends on efficient digestion and absorption from the intestine. Absorption is dependent first on digestion and secondly on the normal function of the mucosal cell. In conditions characterized by abnormal secretion of digestive enzymes or impairment of the function of the intestinal mucosa, varying degrees of malabsorption will occur.

Malabsorption is not uncommon in patients with ileitis. The degree of impairment of absorptive function is dependent on the anatomical distribution and the severity of the disease process. However, the marked nutritional disorders associated with malabsorption in the classical sprue syndrome are not usually so widespread in ileitis. Evidence of impaired absorption may be so subtle that it can only be demonstrated with difficulty using special procedures. In these individuals malabsorption may have little obvious clinical significance for many years. On the other hand, malnutrition resulting from malabsorption in some patients with ileitis may be sufficiently severe to be indistinguishable from that seen in sprue.

Digestion and Absorption

The carbohydrates and starches must undergo complete hydrolysis (digestion) to their constituent monosaccharides before they can be absorbed. The most important monosaccharides in human nutrition are glucose and fructose. During their absorption the glucose and fructose molecules pass through the mucosal cell where they are phosphorylated to form a hexose monophosphate. Phosphorylation provides for a constantly steep gradient in the concentration of these sugars from the intestinal lumen to the mucosal cell. This provides for rapid absorption of these materials, mostly independent of their concentration in the lumen. The enzymatic removal of the phosphate moiety from the sugar occurs at the inner cell barrier. Glucose itself is then liberated into the bloodstream.

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The proteins undergo complete digestion in the lumen to their individual amino acids and in this form they are absorbed. Little is known regarding the biochemistry of amino acid absorption. The rapid rate of amino acid transfer across membranes can hardly be accounted for by passive diffusion; it is probable that an active metabolic cycle is involved.

The digestion and absorption of dietary fat remains a more complex matter and a problem of much controversy. The classic view as presented by Verzar and McDougall (1936)* maintains that following emulsification in the intestine, complete lipolysis or splitting of dietary fat into glycerol and fatty acids is necessary for absorption. Thus glycerol is absorbed as a simple water-soluble molecule and the fatty acids combine with bile to form water-soluble complexes for absorption. Within the mucosal cell the fatty acids combine with glycerophosphate in the synthesis of phospholipid in similar fashion to the changes involving glucose. De-phosphorylation at the inner cell barrier results in the liberation of neutral fat into the systemic circulation. Eighty per cent of absorbed fat is believed to be carried in the lymph to the thoracic duct, there emptying into the bloodstream; the remainder passes by way of the portal blood to the liver.

More recently, Friizer (1952) proposed the partition theory of fat absorption wherein some dietary fat is absorbed without preliminary splitting. The partial hydrolysis of some triglyceride fat provides a fatty acid-bile salt monoglyceride system capable of emulsifying other neutral fat into very fine particles less than 0.5 micron in diameter. The finely emulsified neutral fat (triglyceride) is then absorbed through the intestinal mucosa into the lacteals and passes through the thoracic duct into the systemic circulation where it appears as chylomicrons. On the other hand, the fatty acids are partitioned from the neutral fat and it is claimed that they pass directly into the portal circulation to the liver.

The degree of luminal degradation of dietary triglyceride to its constituent fatty acid and glycerol is the major point of difference between the *lipolytic* and the *partition* theories of fat absorption (see fig. 72). The former theory postulates complete lipolysis while the latter supposes liberation of only part of the fatty acid from the triglyceride.

*Bibliography for this chapter will be found at the end of the chapter page 197-199. All other references listed on page 0-235.

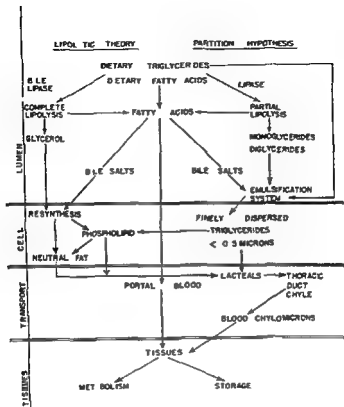


FIG. 72 A. here showing the malabsorption of fat between the lipolytic and partition theories of fat absorption.

At the present time on the basis of studies by Bergstrom and Bergstrom (1950) and by Reiser (1955) it would appear that complete lipolysis is improbable on the one hand and the absorption of triglyceride is unlikely on the other. Actually partial hydrolysis of all triglyceride to mono and diglyceride appear to be the preliminary chemical state necessary for the absorption of fat. The resynthesis of these products to triglyceride within the intestinal cell remains unchallenged as does the lymphatic pathway as the major route of fat transport to the systemic circulation.

From the above it can easily be seen that abnormalities in digestion and subsequently absorption can occur with abnormal changes at various stages involving the digestive enzymes the luminal environment the integrity of either the structural or metabolic properties of the mucosal cell the lacteal and lymphatic transport system and finally the necessary physical contact between the mucosal cell and the products of digestion.

Each of these possibilities can occur alone or in combination in patients with ileitis at various stages in the life history of the disease. The absorption defects and their gross influence on the nutrition of the patient will be discussed below on the basis of personal experience and absorption studies carried out on some 200 patients with ileitis. The effects of malabsorption will be considered as they may contribute to the clinical picture of ileitis.

Gastrointestinal Defects and Malabsorption in Ileitis

Pancreas Dreiling (1957) found evidence of abnormal enzyme secretion of 8 of 26 ileitis patients subjected to secretion stimulation. Only isolated enzyme deficiencies were observed and whether or not these were of sufficient severity to interfere with digestion is not known. The incidence of impaired absorption is far greater in the case of fat than either carbohydrate or protein. Whether this is indicative of a more complex mechanism for fat absorption or is merely a reflection of the larger molecular size of fat is not known. Certainly dietary fat has a greater dependence on its hydrolytic enzyme pancreatic lipase than the other food stuff for their particular enzymes. When known diseases of the pancreas affect enzyme secretion abnormalities in fat digestion and absorption occur most readily even in the absence of evidence of carbohydrate and protein malabsorption.

A relationship between pancreatic malfunction and the etiology of ileitis was first suggested by Avery Jones and Piulley (1949) and further elaborated upon by Cooke (1952). These authors observed certain similarities and relationship between sprue Whipple's disease and celiac disease (all characterized by steatorrhea) and ileitis. They theorized that in the presence of altered lipolytic enzyme activity abnormal products of digestion could conceivably occur which might enter the mucosal cell and initiate the granulomatous lesion of ileitis. A second possibility was based on the conclusions of Hays (1938) that multinucleated giant cell formation was a tissue reaction to interstitial lipolysis and liberation of abnormal fatty acids. Thus some evidence

for abnormal pancreatic enzyme secretion has recently been found which may provide additional weight to the theory that abnormal fat digestion and malabsorption may be involved in the etiology of ileitis as well as a result of it.

The Intestinal Mucosa The mucosal cell is the fundamental absorbing unit and as such it is a highly active metabolic entity. The normal function of any cell is in part dependent on the maintenance of its structural component, not excepting the cellular membrane and vascular supply. The involvement of these structures in an inflammatory and cicatrizing lesion may result in their partial or complete physical destruction. Under these conditions the passage of materials across the cell membrane may not be possible; if it does occur then their transfer through the interior of the cell in the absence of the normal series of metabolic reactions may be blocked. Malabsorption at the cellular level would then result. The pathologic process of ileitis has no limitation in the overall area of intestinal mucosa which may become involved. Theoretically the infiltration of large areas of intestine with a destructive process should result in more severe impairment of cellular function and absorption than when small areas are involved. This is usually found to be the case; however it is not invariably true and the anatomical sites of the lesion as well as the stage in its life history are contributing factors.

Patients with large areas of involvement and advanced disease have been studied who were presented with only minor absorption and nutritional difficulties. These were usually longstanding cases in whom it must be assumed that compensatory mechanisms involving increased function of remaining normal tissue through villus hypertrophy and delayed motility had occurred. On the other hand patients with small areas of intestine involved in a highly inflammatory and active lesion with marked malabsorption have also been studied.

The Site of Lesion The anatomical site of the lesion may also play a major role in determining the extent of malabsorption. Evidence has been reported which indicates the existence of defined lengths of intestine with specialized cells for absorbing one material or another. In 1936 Veznar and McDougal observed that glucose was preferentially absorbed from the proximal half of the small intestine. Mollin (1957) and his co-workers in England have demonstrated in the rat that the ileum is the primary site of absorption of ^{60}Co labeled vitamin B₁₂. This is in agreement with clinical observation of impaired absorption of B₁₂.

From the above it can easily be seen that abnormalities in digestion and subsequently absorption can occur with abnormal changes at various stages involving the digestive enzymes the luminal environment the integrity of either the structural or metabolic properties of the mucosal cell the lacteal and lymphatic transport system and finally the necessary physical contact between the mucosal cell and the products of digestion.

Each of these possibilities can occur alone or in combination in patients with ileitis at various stages in the life history of the disease. The absorption defects and their gross influence on the nutrition of the patient will be discussed below on the basis of personal experience and absorption studies carried out on some 200 patients with ileitis. The effects of malabsorption will be considered as they may contribute to the clinical picture of ileitis.

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presence of the actual diseased tissue may be eliminated. In time following resection the absorption of carbohydrate and protein (and often fat) is partially or totally restored even when several feet of intestine have been removed. Compensatory mechanisms appear to be responsible for this restoration of function (Kogan Schapira Janowitz and Adlersberg 1957). The personal experience of the present author following removal of all but five feet of small intestine has been a persistent intolerance to fat and fat soluble vitamins but normal absorption of carbohydrate protein water soluble vitamins (except B₁₂) and electrolytes.

Hypermotility. Malabsorption may occur in the presence of marked hypermotility associated with active disease limited to a very small portion of the total absorbing mucosa. The cause of impaired absorption in these instances is based on insufficient contact time between the intestinal mucosa and the material to be absorbed. The deficiencies observed under these conditions are not usually limited to single entities but cover the broad spectrum of the diet since the entire food bolus is passing through the length of the intestine at a rate too rapid for any of its constituents to have sufficient contact time with the mucosal surface to be absorbed.

The Measurement of Malabsorption

The oral tolerance test has been the procedure most widely used to study absorption from the intestine in ileitis. This method involves the determination of the concentration of a test substance in the blood or urine after an oral test dose of that substance or its precursor.

The interpretation of a tolerance test as a measure of intestinal absorption requires some degree of caution. The blood concentration is the resultant of absorption utilization and mobilization from storage depots and is not merely a measure of absorption alone. In addition the results of a tolerance test utilizing a single test substance must be expressed in terms of the material fed rather than in terms of overall absorptive function since the intestine varies in its capacity to absorb different substances particularly under abnormal conditions.

The use of balance studies in which the quantitative estimation of intake and output is performed is probably the most accurate means for studying absorption. The cost of the special facilities necessary for such studies has limited their use.

Recently radioactive isotope labeled materials have become readily available and these have stimulated new interest in the possibility of

in patients in whom the ileum has been surgically removed. In 1954 Kremen, Linner and Nelson carried out fat balance studies in dog after removal of distal or proximal lengths of intestine from gastrointestinal continuity. Their studies indicated that steatorrhea and weight loss was greater with removal of the distal small intestine. They concluded that the distal small intestine was the major site for the absorption of fat. Benson (1956) and his group fed I^{131} labeled olive oil to rats and found that a specific portion of the third quarter of the mucosa of the jejunum contained the maximum activity. Turner (1956) fed both dogs and rats I^{131} and C^{14} labeled neutral fats and observed a maximum activity of labeled fat from the duodenum beginning at the ampulla of Vater and continuing to the distal jejunum (fig 73). The observations were in agreement with the early reports of Claude Bernard (1856) who described the occurrence of milky chyle after a fatty meal immediately distal to the ampulla of Vater in dogs and rabbits. These results appear to be in conflict with those reported both by Benson and by Kremen. However it seems difficult to relate their findings to the frequently reported observation of maximal lymphatic lactescence indicative of fat absorption in the proximal intestine after a fat meal. The clinical significance of these findings is presently being investigated in this laboratory with patients undergoing resection at various levels of the small intestine.

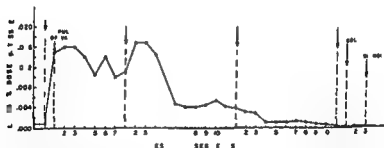


FIG 73 The residual I^{131} lipid activity in serial sections of the gastrointestinal tract 3 hours after the ingestion of 20 Gm I^{131} triolein

Resection of portions of the small intestine in ileitis results in the reduction of effective absorbing mucosal tissue. Basically the effect is similar to that observed when similar areas of the mucosa are destroyed by the disease process, although certain secondary effects due to the

presence of the actual diseased tissue may be eliminated. In time following resection the absorption of carbohydrate and protein (and often fat) is partially or totally restored even when several feet of intestine have been removed. Compensatory mechanisms appear to be responsible for this restoration of function (Kogan, Schapira, Janowitz and Adlersberg, 1957). The personal experience of the present author following removal of all but five feet of small intestine has been a persistent intolerance to fat and fat soluble vitamins but normal absorption of carbohydrate, protein, water soluble vitamins (except B₁₂) and electrolytes.

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Recently radioactive isotope labeled materials have become readily available and these have stimulated new interest in the possibility of

obtaining quantitative measurement of intestinal absorption utilizing specific substances in oral tolerance tests

Carbohydrate Absorption The glucose tolerance curve is not very useful as a measure of absorption in these cases because of its marked dependence on other variables such as liver adrenal and pancreatic function. No diagnostic features were noted using this procedure in 112 patients with ileitis. The results in 85 per cent of the cases were within normal limits but considerable variability was observed in any one individual tested on several occasions. The rapidity with which glucose is absorbed from the upper small intestine (Verzar and McDougall 1936) apparently assures normal absorption except where malfunction involves the whole intestinal mucosa such as in sprue.

The use of the pentose sugar d(+)-xylose as the test substance has provided a more consistent means for studying absorption (Brien Turner Watson and Geddes 1952). The resultant curve in 100 normal subjects and in 60 patients with ileitis studied was highly reproducible on separate occasions in the same individual. In the abnormal group deviation of the test curve from the normal mean was usually closely related to the

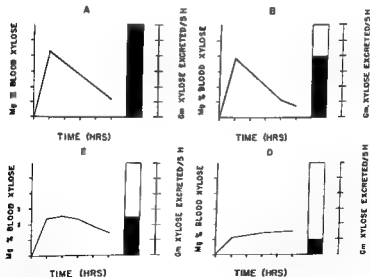


FIG. 74 The characteristic blood xylose changes and urinary xylose excretion following the ingestion of 25 Gm of D(+)-xylose in (A) normals (B) regional ileitis (C) ileocecalitis and (D) sprue

extent of pathologic involvement of the intestinal mucosa as determined at operation or by roentgen examination.

The sensitivity of the test to changes in absorption was highly significant. A flattened blood and urine test curve often preceded gross clinical or roentgen evidence of the disease process. The procedure has gained wide acceptance as a single diagnostic screening test for condition such as sprue, celiac disease and ileitis. Its particular value lies in differentiating borderline malabsorption where overt clinical evidence is not yet evident (figs 74 and 75).

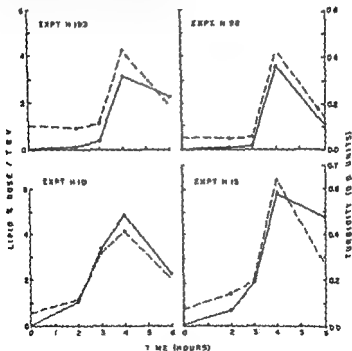


FIG 75 The plasma lipid activity (—) and OD (---) changes in 4 normal human after the ingestion of a 40 Gm 1 trial meal.

The starch tolerance test has greater value as a measure of adequate carbohydrate digestion than as a measure of intestinal absorption. The procedure involves the oral administration of the polysaccharide (starch)

obtaining quantitative measurement of intestinal absorption utilizing specific substances in oral tolerance tests

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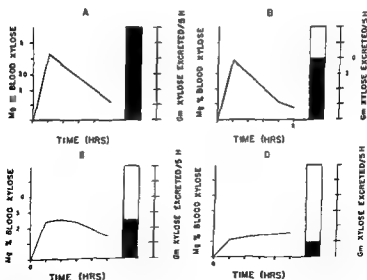


FIG. 74 The characteristic blood xylose changes and urinary xylose excretion following the ingestion of 5 Gm of D(+)-xylose in (A) normal (B) regional ileitis (C) ileo jejunitis and (D) sprue

of calculated total fat intake. This is in contrast to the older 12 day pooled stool collection program and the fractional determination of fecal fat content.

By this method 90 per cent or more of dietary fat is normally absorbed. Steatorrhea occurs when less than 85 per cent of the fat intake is absorbed. The contribution of endogenous fat to the fecal fat content cannot be adequately determined by this procedure and the role of such fat in the etiology of steatorrhea remains a point of controversy.

In ileitis the fecal fat content is elevated beyond normal limits in a majority of cases. Cooke (1955) observed steatorrhea in 45 of 57 cases studied by this technique. In nonoperative patients with involvement of the jejunum or upper ileum steatorrhea was invariably found. When the disease was limited to the distal ileum in the one patient from whom 5 feet of distal ileum had been removed there was no evidence of steatorrhea. Thus impaired fat absorption does not necessarily follow resection of certain areas of the small bowel. These findings lend considerable support to the observation that the ileum plays a minor role in the normal process of fat absorption.

Fat Tolerance Tests. Butter, fat, olive oil and other dietary fats have been orally administered and the changes in the plasma lipid concentrations chemically determined. The large volumes of blood necessary and the time consuming chemical analyses involved make this technique impractical for repeated serial testing in most instances. This type of fat tolerance test is rarely employed at the present time.

Vitamin A. The vitamin A tolerance test has been the most popular measurement of fat malabsorption because of its consistency and simplicity. This has been further stimulated by the work of Legerton, Texter and Ruffin (1953) who showed a direct correlation between fat absorption and vitamin A absorption. Adlersberg and Sobotka (1943) reported little impairment of vitamin A absorption in ileitis in contrast to sprue where the tolerance curve is usually flat. Hogan et al. (1957) found that the vitamin A tolerance curve was fairly normal in several patients following massive resection but this was not consistent. The vitamin A tolerance curve as an index of fat absorption should be read with some caution in the absence of other measures since it does not always follow the fat absorption pattern.

Radioactive Labeled Fats. Radioactive iodine (I^{131}) labeled fat have been shown to be absorbed in similar fashion to ordinary unlabeled fats and a method has been developed for their rapid and simple measure-

followed by measurement of the changes in blood glucose concentration. Galactose has also been used as the test substances in these procedures but this has doubtful advantages over glucose.

Protein Absorption The amino acids are readily absorbed under all but the most abnormal conditions and their use in oral tolerance tests has not been very informative. Nitrogen balance studies provide the best means for studying protein absorption. Glycine is easily measured in blood by a simple colorimetric technique and it has been used clinically in a tolerance test. In 50 cases of ileitis and in 42 patients with partial gastrectomy little consistent evidence of impaired glycine absorption was observed. Even in sprue with evidence of gross malabsorption the glycine tolerance curve was often within normal limits. The oral administration of gelatin with subsequent determination of the changes in blood glycine concentrations has some value in the study of pancreatic (trypsin) function but is of little specific value in studying absorption from the intestine.

Ruffin (1956) and his colleagues have employed I^{131} labeled albumen for this purpose with some success. Radioisotope methods are more convenient than chemical methods when properly used but the labeled proteins presently available that could provide valuable information on protein absorption have not been appropriate for widespread human application.

Fat Absorption The measurement of fat absorption has been the subject of intense interest in recent years. The reason for this is probably two fold: steatorrhea has become increasingly important as an early and troublesome complication in diseases of the intestine. Quite recently quantitative and convenient investigative procedures which were previously lacking have been developed to study fat absorption in man. The great vacuum which existed in our knowledge of fat absorption and metabolism in man was a direct result of this paucity of adequate methodology.

The availability of radioactive labeled fats on the one hand and improved chemical and physical analytical procedures on the other now make possible certain human studies which were previously limited to animals.

Fat Balance The method of Van de Kamer (1949) and his group for measuring fat absorption by the balance technique represents a distinct improvement over older procedures. Here the stools are collected on a 24 hour basis and the total fatty acid content measured by a rapid and simple chemical procedure. The results are expressed as a percentage

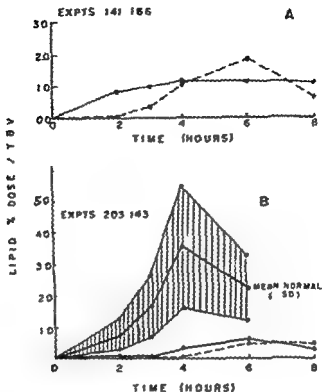


FIG. 76. The lipid tolerance curves in patients after (A) resection of ileitis of terminal ileum and terminal ileitis and (B) after resection of the entire ileum in diffuse ileitis and the mean normal curve (\pm SD).

resection the 48 hour stool values were 19 per cent and 31 per cent of the dose.

The results using chemical analysis of fecal fat or triolein levels are comparable; the latter may well serve as a simplified substitute for tedious chemical analyses or as a supplement for confirmation of special studies.

Trioleic acid has been used in similar fashion to triolein as a means of differentiating steatorrhea due to intestinal (mucosal) disease. The trioleic acid tolerance curve is essentially normal in pancreatic steatorrhea while that of triolein is not. In ileitis or sprue with steatorrhea neither the trioleic acid nor the triolein curves reaches

ments in small volumes of plasma (Turner 1956) The I^{131} triolein and the I^{131} -oleic acid tolerance tests have been used to study fat absorption in 92 patients with steatorrhea resulting from ileitis (46) pancreatic insufficiency (42) or sprue (4)

The measurement of an isotope like I^{131} has many advantages over conventional chemical procedures including greater accuracy and simplicity of determination In addition any increment in the I^{131} lipid levels in the plasma can be definitely attributed to the administered material in contrast to the use of material indistinguishable from endogenous tissue lipids

The normal mean I^{131} triolein blood tolerance curve reaches a maximum value of 4 to 6 per cent of the administered dose per total blood volume in 4 hours (fig 75) In 46 ileitis patients the value rarely exceeded 1.2 per cent In each of 8 patients with previous resection of portions of the ileum the I^{131} triolein tolerance test was repeated on three occasions The maximum peak was consistently less than 1 per cent (fig 76) Subsequently each of these patient underwent further surgery for recurrent disease

The invariable finding of impaired absorption of I^{131} triolein in ileitis may not be a true reflection of the patient's capacity to absorb dietary fat Weijers and Van de Kamer (1950) showed that saturated fatty acids may be selectively rejected by the abnormal intestine while unsaturated fatty acids may be well absorbed even in steatorrhea When triolein is labeled with I^{131} the unsaturated bonds of the constituent fatty acids (oleic acid) are saturated by the halogenation Nevertheless the procedure as outlined and under these conditions is a sensitive method for measuring fat absorption

The fecal fat level of I^{131} triolein vary inversely as the blood levels after the I^{131} triolein test meal When the tolerance curve is depressed the fecal activity is high Some workers have preferred to measure the fecal I^{131} triolein activity and this has certain advantages The limitations in the meaning of a blood tolerance curve are overcome and in addition the sample may be measured directly without previous preparation On the other hand fecal studies involve stool collections which are not always possible or practical

McKenna Bourne and Matzko (1957) have compared both blood and fecal I^{131} triolein level in normals and in patients with steatorrhea They found less than 4 per cent of the ingested labeled fat in the 72 hour stool of normal subjects In two ileitis patients with previous

of its long half life. The availability of a short lived calcium isotope would be a valuable aid to such studies.

Effects of Malabsorption

Malabsorption is normally a subtle symptom in the majority of patients with ileitis. However, subtle deficiencies of this nature result in gross effects if they are not corrected or compensated for over long periods of time.

The systemic effects of malabsorption may be resolved under the heading of malnutrition. In ileitis the picture is one of chronic progression of these effects in terms of their severity and anatomic distribution. In addition, individual deficiencies and malfunction tend to become further complicated when they give rise to secondary disturbances in a cause and effect relationship. For example, even if protein absorption is normal, the presence of steatorrhea may result in weight and energy loss and the breakdown of the protein sparing mechanism and secondary protein deficiency by the conversion of dietary protein to fat and carbohydrate for metabolic purposes. Unless sufficient carbohydrate and protein are fed under these conditions, the depletion of existing tissues coupled with impaired synthesis of new tissues will result in a disastrous chain of events.

Impairment of fat absorption is the most common form of malabsorption observed in ileitis. The loss of fat soluble vitamins A, D, K, and E may result in any of the known clinical entities peculiar to their deficiency.

Electrolyte disturbances are usually associated with potassium or calcium loss in these patients. Thus, generalized muscle atonia and tetany, respectively, have been observed in certain instances. Osteomalacia associated with calcium loss secondary to protein depletion and vitamin D loss with steatorrhea has been reported.

With watery diarrhea and the consequent loss of the water soluble vitamins, the classical signs of B complex deficiency are commonly observed. These can be adequately controlled by appropriate parenteral therapy.

BIBLIOGRAPHY FOR CHAPTER 17

1. Adlesberger H and Soboth H. Fat and vitamin A absorption in jejunitis. *Gastroenterology* 1: 357, 1943.
2. Benson J A, Chandle G W, Van der Nuy F E and Gagnon J O.

normal levels. The defect in pancreatic deficiency is in lipolysis which only affects triglyceride whereas the defect in ileitis and sprue is a fundamental absorption defect at the cellular level.

Vitamin B₁₂ Absorption The absorption of vitamin B₁₂ has been studied by three techniques all of which confirm the widespread impairment of vitamin B₁₂ absorption in ileitis and particularly in the presence of steatorrhea. Again the use of radioactive labeled material Co⁶⁰B₁₂ has simplified and extended clinical studies of intestinal absorption.

Heinle, Welch, Scharf, Meacham and Prusoff (1952) gave 0.5 µg doses of Co⁶⁰B₁₂ and measured the fecal excretion of radioactivity. The method of Schilling (1953) involves the administration of 5 µg of Co⁶⁰B₁₂ followed by a parenteral injection of 1000 µg of non-radioactive B₁₂. If the Co⁶⁰B₁₂ has been absorbed considerable radioactivity can be measured in the urine whereas none will appear if it has not been absorbed. More recently Glass, Boyd, Gellin and Stephenson (1954) have shown that Co⁶⁰B₁₂ taken by mouth accumulates in the liver and that the radiation can be counted by directional scintillation counting over the liver.

The method of Glass et al (1954) appears to be the most practical procedure with which to study vitamin B₁₂ absorption in patients with malabsorption. To differentiate vitamin B₁₂ malabsorption in pernicious anemia from that observed in sprue or ileitis a source of intrinsic factor is given with the test dose of Co⁶⁰B₁₂. In pernicious anemia the B₁₂ will be normally absorbed under these conditions but intrinsic factor has no effect on the absorption of vitamin B₁₂ in intestinal disease.

Damage to the mucosa of the ileum by disease or its surgical removal would be expected to result in vitamin B₁₂ malabsorption since the ileum appears to be the site of vitamin B₁₂ absorption.

Electrolyte Absorption The presence of steatorrhea or watery diarrhea results in the loss of electrolytes in the stool. This phenomenon has been intensively studied by Cooke (1955) who found that potassium loss was the most significant observation. The fecal determination of the electrolyte elements remains the best method for determining their absorption. The use of radioactive K has not been completely satisfactory in terms of a tolerance test using this isotope.

Ca⁴⁵ has been used in this laboratory in studies of the absorption of calcium in dogs with experimental steatorrhea. Fecal calcium loss is increased markedly in the presence of steatorrhea. The use of this isotope in human subjects is not compatible with present safety regulations because

- 20 Schilling R F Intinsic factor tests The effect of gastric juice on the urinary excretion of radioactivity after the oral administration of radioactive vitamin B₁₂ J Lab & Clin Med 4: 360 1951
- 21 Turner D A The absorption transport and disposition of fat Ph.D. thesis University of Western Ontario London Canada 1956
- A simplified procedure for studying fat absorption and utilization using I¹⁴C labeled triolein or oleic acid Clinical Research Proceedings 5: 106 1957
- 22 Van de Kamer J H Huinink H Ten Bokkel and Wejer H A Rapid method for the determination of fat in feces J Biol Chem 161: 347 1949
- 23 Vezar M and McDougall E J Absorption From The Intestine London Longmans Green 1936

Studies concerning the site of fat absorption in the small intestine of the rat *Gastroenterology* 30 53 1956

- 3 Bergstrom S and Borgstrom B The intestinal absorption of fats *In* *Progress in the Chemistry of Fats and Other Lipids* London Pergamon Press 1955
- 4 Brien F S Turner D A Watson E M and Geddes J H A study of carbohydrate and fat absorption from the normal and diseased intestine in man The absorption and excretion of D xylose *Gastroenterology* 20 287 1952
- 5 Cooke W T Steatorrhea and regional ileitis *In* *Modern Trends in Gastroenterology* Ed Avery Jones London Butterworth and Co Ltd 1952
- 6 — Nutritional and metabolic factors in the etiology and treatment of regional ileitis *Ann Roy Coll Surgeons England* 17 137 1955
- 7 Dreiling H A The pancreatic secretion in the malabsorption syndrome and related malnutrition states *J Mt Sinai Hosp* 24 243 1957
- 8 Frazer A C The mechanism of fat absorption *In* *Biochem Soc Symp* 9 Cambridge Cambridge University Press 1952
- 9 Glass G B J Boyd L J Cellin G A and Stephenson L Uptake of radioactive vitamin B₁₂ by the liver in humans test for measurement of intestinal absorption of vitamin B₁₂ and intrinsic factor activity *Arch Biochem* 51 251 1954
- 10 Hales G M quoted by Cooke W T *Arch Path* 26 1183 1938
- 11 Heinle R W Welch A D Scharf V Meacham G C and Prusoff W H Studies of excretion and absorption of Co⁵⁷ labeled vitamin B₁₂ in pernicious anemia *Trans Am Physicians* 65 214 1952
- 12 Jones A F and Paulley J W Intestinal lipodystrophy *Lancet* 1 214 1949
- 13 Kogan E Schapira A Janowitz H D and Adlerberg M Malabsorption following extensive small intestinal resection including inadvertent gastro-ileostomy *J Mt Sinai Hosp* 24 399 1957
- 14 Kremen A J Linner J A and Nelson C H An experimental evaluation of the nutritional importance of proximal and distal small intestine *Ann Surg* 140 439 1954
- 15 Legerton C W R Texte C E and Ruffin J M Observations on the vitamin A tolerance test as an index of fat absorption *Gastroenterology* 23 447 1953
- 16 McKenna R D Bourne R H and Matzko A The use of I¹³¹ labeled fat in the study of fat digestion and absorption in normal individuals and in patients with decrease of fat absorption *Gastroenterology* 32 17 1957
- 17 Mollin H L personal communication 1957
- 18 Reiser R Recent studies on fat digestion and absorption *Clin Chem* 1 93 1955
- 19 Shingleton W W Well M H Baylin G J Ruffin J M and Sander A The use of radioactive labeled protein and fat in the evaluation of pancreatic disorder *Surgery* 38 134 1955

- 20 Schilling M F Intrinsic factor study The effect of gastric juice on the primary excretion of radioactivity after the oral administration of radioactive vitamin B₁₂ J Lab & Clin Med 52 860 1953
- 21 Turner D A The absorption and partition of fat Ph D thesis The University of Western Ontario London Canada 1956
- 22 — A simplified procedure for studying fat absorption and utilization using I labeled triolein oleic acid Clinical Research Proceedings 5 106 1957
- 23 Van de Kamer J H Huisink H Ten Bokkel and Weijers H A Rapid method for the determination of fat in feces J Biol Chem 171 347 1949
- 24 Verzar F and McDougall E J Absorption From The Intestine London Longmans Green 1936

Chapter 18 : Prognosis and Treatment of Ileo-Jejunitis

OF THE 70 CASES in this present series 50 were followed for from 1 to 25 years unfortunately 20 were lost to follow up Even so it might be interesting to see what happened to those successfully followed

TABLE 18

FOLLOW UP OF MEDICALLY TREATED CASES (32 CASES)

<i>Years</i>	<i>Good</i>	<i>Poor</i>	<i>Died</i>
0 1	3	2	
1 ~	1	1	4 deaths (medical)
2 3	0	1	directly
3 4	3	1	attributable
4 5	3	0	to the disease
5 10	7	2	
10 15	3	0	
15 20	0	0	
20 25	1	0	
	—	—	
	21	7	

TABLE 19

FOLLOW UP OF SURGICALLY TREATED CASES (18 CASES)

Short circuiting procedure	1 case poor result
Resection	4 cases good result
	9 poor
	4 deaths

All death occurred immediately postoperative

Obviously surgery has little place in ileo jejunitis except as an emergency procedure for obstruction Attempt at massive resections are disappointing and are associated with a high operative mortality Four cases that survived massive resection were well and were not showing electrolyte imbalance despite small segment of persisting jejunum On the other hand medical conservative treatment is most promising with a high percentage of improvement and with restitution to fair health and good efficiency

In 1941 Crohn and Yunich published a series of 38 cases of ileo jejunitis 13 of which were well 6 clinically in fair condition 7 poor 6 deaths and in 6 no follow up. It would seem then that our latest the present (1957) series shows better end results possibly due to the extensive use of the steroids. A typical case is that of a young man 17 years of age who was being observed for ileo jejunitis with diffuse involvement of the jejunum and upper ileum with active symptoms. Five years later a follow up showed marked clinical improvement cessation of active symptoms and a gain of 50 pounds in weight. On re x ray the jejunal pattern was seen to be restored to normal the upper ileum was contracted the mucosal pattern disarranged thus indicating the greater susceptibility of the upper jejunum to self healing. This observation has been repeatedly made in this series namely clinical cure though persistent radiographic evidence of a burnt-out disease.

Such instances of apparent cure of jejunitis confirmed by exploratory operation or by roentgenographs have previously been independently noted by Pessagno by Wilensky by Sussman and Wachtel and by Gross in individual cases.

On the other hand the severity of the disease is indicated by the fact that in this series 7 cases were only fair or poor and above all 4 had fatal terminations as a result of perforation (1 case) of sepsis (Friedlander bacillus) (once) of inanition (1 case) of intercurrent disease (1 case). The unsatisfactory clinical outcome in 7 cases including 4 deaths is clear evidence of the severity and persistence of the disease process in progressively undermining nutrition and protein and mineral reserves.

The fact that 21 cases did improve sufficiently as to resemble clinical cure is impressive and does indicate that self healing in high jejunitis is possible. The regain of weight in these cases is impressive and the surcease from fever diarrhea and anemia most striking.

Medical Therapy

The conservative treatment of ileo jejunitis applies principally to the type in which diffuse involvement of the entire small bowel exists or to those in which the disease affects such large stretches of upper ileum and the whole jejunum as to preclude any idea of surgical intervention. The conservative approach to therapy is aimed at establishing some degree of partial sterilization of the intestinal tract by the use

of antibiotics and to maintain nutrition and electrolytic balance in the plasma and to combat anemia and vitamin deficiencies

As antibiotics penicillin is useless streptomycin is possibly of some avail In the febrile cases particularly where suppurative complications mesenteric abscess and fistula or perirectal manifestations are suspected the broad spectrum antibiotics are of greatest utility It is difficult to say which of these antibiotics gives the best results if there is actually any true basis for preference Aureomycin and terramycin should not be employed because of their tendency to increase the severity of the diarrhea by suppressing the normal flora of the intestinal tract Achromycin erythromycin Mystelcin disturb least and give better results it is quite possible that one of the newer broad spectrum antibiotics of which there seems an unending list will surpass others in reducing fever and secondary infection without producing untoward intestinal side effects

The corticosteroids offer the best approach to direct therapy over a long period of time ACTH by injection is rarely needed except in febrile cases cortisone hydrocortone or meticorten or prednisone given by mouth in doses of 15 to 25 milligrams daily over long periods is best indicated These dosages seem small in comparison to the dosage employed by many other clinicians In fact we have seen cortisone or its analogous products given in dosage of up to 75 to 150 milligrams daily and according to these authors with excellent results One of the best cases we saw one of diffuse ileo jejunitis with complete restitution to health and efficiency was maintained on this high dosage for many months It is our own view that the dosage should be more moderate much more so but prolonged over months and if necessary years

Nutrition is maintained by a liberal soft nonroughage diet not too strictly construed High protein high carbohydrate elements in the diet are stressed meats fish chicken eggs milk pureed vegetables fruit juices and bread and butter being forced (see pp 122 124) The protein content of the diet may be reinforced by the use of the protein hydrolysates up to 4 to 6 ounces a day being urged on the patient The newer commercial preparations are no longer bad tasting they are actually palatable and tend to maintain and restore nitrogen balance Occasional transfusions of whole blood or of plasma aid in overcoming hypoproteinemia raise the total proteins of the blood and restore when plentifully administered over a long period of time the relationship between the albumin and globulin fractions of the plasma

The intramuscular injection of crude liver extract plus vitamin B

complex 2 cc of each plus II 50 micrograms every day or every other day tend to overcome anemia encourages blood formation and replaces the deficiency in vitamin absorption which result from the damaged intestinal tract. Even though the beneficial effect of such injection are not evident in ileo-jejunitis as in prue they should continue to be regularly administered.

Fresh air sunshine and much rest particularly at the seashore or in the mountains often act beneficially to effect general improvement in weight and strength.

Surgical Intervention

The indications for surgical interference are limited to those cases in which the lesion is localized to one or more isolated segments of the small bowel such as group 1 and 2 possibly and group 6 more likely (see chapter 16 page 160).

In this series of 70 cases 18 were subjected to a radical procedure. The follow up of these cases has already been noted in table 19. A few observed good results were obtained in only 4 cases 4 additional deaths and 9 poor results certainly do not give an encouragement for radical surgery in ileo-jejunitis. And yet surgical intervention is warrantable and indicated when the true nature of the disease is in doubt or the extent and implication of the disease cannot be radiographically established with certainty or where the question of obstruction has been raised. A case may seem to be segmental or localized in extent but at exploration may be discovered to be of the diffuse type not amenable to resection. Or a case considered diffuse and probably incapable of surgical help may be determined at exploratory operation to be segmental and capable of resection.

Where no benefit is being derived from conservative medical treatment an exploratory operation is often justified. The removal of the appendix is a superfluous manipulation fortunately in ileo-jejunitis appendectomy rarely results in abdominal wall fistula.

In group 1 where the disease is an extension upward of ileitis so as to invade and include the jejunum radical surgical procedure offers scant hope of success.

In group 3 4 and 5 those cases in which the disease invades the whole of the jejunum and much or all of the ileum the encouraging attitude toward reckless excision of the involved intestine holds equally true.

Massive resection of the small bowel with the sacrifice of most

of its length has been occasionally encountered in the literature not for ileitis or jejunitis but more often for strangulation for volvulus for superior mesenteric vein thrombosis or for intussusception (Copwell Gorse)

The average length of the small intestine varies under normal conditions from 18 to 26 feet averaging 21 feet 6 inches

Gray's Anatomy—20 feet 6 inches

Rost—18 to 26 feet averaging 19 feet

Treve—22½ feet in the male 23¼ feet in the female adult

Sarnoff felt that half of the small intestine could be sacrificed without unduly endangering life and he quoted 5 cases in which 18 17½ 17 16 and 13¼ feet of small bowel had been removed all survived the operation but died later Pate reported a case in which 12½ feet of small bowel were removed for a traumatic strangulation of the mesentery only 12 inches of jejunum remaining the patient was well four weeks later In a case reported in 1940 (Todd Dittenbrandt and Montague) all but 3 feet of jejunum had been surgically removed resultant carbohydrate metabolism was normal proteins not so well absorbed (67 75 and 76 per cent in three periods) tetany was prevented by liberal administration of calcium and vitamin D In their study of metabolism in the cases 25 per cent of the protein intake and 45 per cent of the fat intake were lost in the feces a total loss of 25 per cent of the caloric value of the ingested food The fecal fat showed much free fatty acids indicating good splitting but poor absorption

Coleman and Bennett report massive small intestinal resection with survival the resection involving 6 feet 7 inches in one case 14 feet 8 inches of small bowel in another case Prioleau also supports the view that massive resection of the small intestine is possible with survival under fortunate circumstances He reports 2 cases one with a 40 per cent resection and one with a 53 per cent resection of the small bowel with survival although the latter case died four months later Elman and Reed report the resection of all but 3 feet of proximal jejunum and also the right half of the colon the patient gained 50 pounds of weight and experienced normal bowel function The results of human resections indicate that approximately two thirds of the small bowel can be removed without serious risk of life (Berman et al) They report the removal of all but 18 inches of the jejunum and the right half of the colon for ergot poisoning and superior mesenteric vein thrombosis with complete recovery the daily postoperative defecations were limited

to three formed stools per twenty four hours Althausen reported the resection for mesenteric thrombosis of 435 cm of the jejunum The patient survived the operation tolerably well with retained nutrition as proved by extensive studies of metabolism and of food absorption

While such massive resection of the small bowel are thus shown to be possible with survival the attempt to apply that principle to diffuse ileo-jejunitis would likely be associated with an extremely high mortality because of the previous state of malnutrition and anemia and is scarcely to be encouraged

In group 6 the cases with high and isolated segmental involvement of the jejunum localized resection of the lesion is not only possible but is highly successful Such was the outcome in our 3 cases in the present series Johnson resected 3 feet of upper jejunum beginning at the fosa of Treitz for localized jejunitis Brewster resected 2 feet of jejunum for a lesion beginning 2½ feet caudad of the fosa of Treitz Both cases made complete recoveries Spellberg and Gray performed a gastroenterostomy for a traumatic segmental jejunitis because of poor result denoted by delay in the proximal loop a secondary resection was performed with a successful outcome Gendel and Beaver had an identical experience Lyons and Garlock resected 10 inches of upper jejunum for localized jejunitis whose upper limit was the fosa of Treitz with good result The case of Koenig was equally successful after a resection of 3 feet of jejunum

In high jejunitis multiple segments of involvement are not uncommon It often becomes necessary to treat or resect each individual focus of disease as an independent lesion in order to achieve a successful outcome Dixon cites a striking case of recurring obstruction from multiple non neoplastic tumefaction of the jejunum An interesting insight into the life history of localized jejunitis may be gained from the study of a case published by Husebye In 1928 a 49 year old man was operated on for an acute phlegmonous jejunitis an entero-anastomosis was performed at the ileo-jejunal junction The operation was followed by a long period of apparent good health In 1945 or seventeen years later the reappearance of heartburn and abdominal cramps was followed by the clinical picture of an acute abdomen The radiographic examination showed the upper jejunum to be irregular narrowed tortuous the upper jejunum and the duodenum were distinctly dilated and retained barium At operation the roentgenographic findings were confirmed the jejunum was diffusely scarred the lumen contracted

and the proximal bowel and duodenum and stomach abnormally dilated. A gastro jejunostomy and a jejuno jejunostomy were performed; the patient succumbed to the high intestinal obstruction and the extensive surgical procedures. Apparently, in this case, in spite of the entero-anastomosis, the healing of the short-circuited segmental jejunitis had resulted in scar tissue contraction and in high intestinal obstruction.

In group 2, where a high jejunitis is associated with an independent and similar lesion in the terminal ileum, the operation of choice is localized resection of the upper jejunal lesion and a short-circuiting of the lower ileal lesion (ileo-transverse colostomy with transection of the proximal ileum above the diseased area). Our previous (1949) series included three instances of combined lesions successfully operated on by local resection of the terminal ileal segment; all of them successfully accomplished.

In summary, it will be seen that surgical intervention in ileo-jejunitis is advocated both as an exploratory procedure and as a means of attack in those cases of high jejunitis with or without distal ileal involvement. In the localized or segmental forms of jejunitis, surgical intervention results frequently in restoration of health and intestinal function.

Chapter 19 Ileocolitis

by Harry Yarnis, M.D.*

BOTH ILEITIS and non specific or idiopathic ulcerative colitis constitute allied diseases and if not identical in nature at least belong to the same family. The etiology of neither disease is known both occur in young people and have the same sex distribution both have the same general life span of extension with recurrences and are characterized by such common complications as rectal suppurative phenomena erythema nodosum fever hypoproteinemia and secondary anemia. Both occur in the pure form in the great majority of cases but certain mixed form must be recognized. Thus universal ulcerative colitis will involve the terminal portion of the ileum in about 25 per cent of the case. Segmental or right-sided ulcerative colitis will involve the terminal ileum in a much higher number of instances. Crohn, Garlock and Yarnis having reported involvement of the terminal ileum in 40 per cent of 77 cases of segmental colitis. The ileitis in these cases is not granulomatous in nature but ulcerative or exudative in type and is due to regurgitation of the infected colonic contents through an incompetent ileo-cecal valve. Such ileitis does not extend aborally by skip-lesion does not cause obstruction and is not associated with internal or external fistula.

On the other hand true regional enteritis infrequently crosses the ileocecal valve. However only two years after the original description of terminal ileitis in 1932 Colp published a report of a case in which he resected a nonspecific granuloma of the terminal ileum and cecum. Subsequently similar cases were added and in 1936 Crohn and Rosenak cited 60 cases of regional ileitis in 9 of which simultaneous involvement of the colon was found to exist. Mucik further described a case in which 18 inches of ileum 3 inches of cecum and 3 inches of sigmoid were simultaneously involved. An ileo-ascending colostomy was performed on the right side. Mikulicz procedure on the left colon with successful outcome. Pesagno (1937) reported regional ileitis with in-

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involvement of the cecum Pugh reported 9 cases of ileitis with evidence of extension of the pathologic process into the large bowel In 6 the cecum in 2 the sigmoid and in one the transverse colon were implicated The parenthood of the combined form of the disease seems to rest in the terminal ileum Pemberton and Brown pointed out that if an ileocolostomy be performed for a combined lesion at subsequent exploration the colonic lesion will be found healed only the ileitis constituting the residual focus of the disease This is an astute observation which is amply confirmed in the life histories of several cases in this present series Clark and Dixon found that in 23 out of 44 cases of regional enteritis observed the large bowel mainly cecum and ascending colon were involved with the terminal ileum And yet they distinctly say "The distal portion of the ileum appeared to be the original site of invasion of the disease in practically all cases"

The highest incidence of colonic involvement in regional ileitis was reported in 1951 by Rappaport Burgoyne and Smetana who published a report of 100 cases of regional ileitis with extension into the colon in 55 instances However in many of these cases the granulomatous extension into the colon was minimal and could be detected only by microscopic technique In our personal experience granulomatous involvement of the colon in regional ileitis has not been common However minimal involvement of the cecum and ascending colon by granulomatous disease is frequently secondary to internal fistulas which originate in the diseased ileum and terminate in the colon

The granulomatous nature of regional ileitis and the inflammatory character of the typical case of ulcerative colitis are well established However there is no such agreement concerning the pathology of segmental or regional colitis Warren and Sommers regard these two diseases as morphologically different and have never seen a case of granulomatous colitis On the other hand Newman and Dockerty reported 25 resected specimens of segmental colitis in which there was a marked thickening of the entire colonic wall and microscopically presented as nonspecific granulomatous process Wells reported cases of segmental colitis in which he described the typical microscopic appearance of a granuloma with giant cells and epithelioid tubercle formation in the colon In fact the gross and microscopic appearance in these cases of segmental colitis was so similar to granulomatous or regional ileitis that he chose to call this type of segmental colitis Crohn's disease of the colon

Brooke and Cooke described a form of ileocolitis due to malabsorption and dysfunction of the small intestine resulting in poor fat absorption and steatorrhea. This is followed by superficial ulceration of the ileum which progresses through the ileocecal valve to involve the colon. It is necessary to recognize this type of deficiency disease because surgical intervention is precluded due to the progressive nature of the malady.

In our experience the pathologists have almost always reported resected specimens of segmental colitis as ulcerative in nature. However in the past two years we have seen 4 cases of typical granulomatous disease of the colon. In all these cases there was marked thickening of the colonic wall in many instances there were skip areas and the microscopic appearance revealed fibrosis, giant cell system and epithelioid cells or tubercles.

Therefore it appears that regional ileitis may be associated either with ulcerative colitis or with granulomatous colitis. The term combined ileocolitis means the presence of granulomatous ileitis and ulcerative colitis. When granulomatous ileitis combines with granulomatous colitis the best term we believe is, granulomatous ileocolitis.



TERMINAL ILEUM AND
PROXIMAL COLON
19 CASES



TERMINAL ILEUM AND
TRANSVERSE COLON
2 CASES



TERMINAL ILEUM AND
ENTIRE COLON EXCEPT RECTUM
10 CASES



DIFFUSE ILEOCECUM AND
ENTIRE COLON EXCEPT RECTUM
6 CASES



TERMINAL ILEUM AND
DISTAL COLON
5 CASES



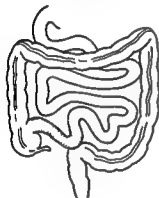
TERMINAL ILEUM AND
ENTIRE COLON INCLUDING RECTUM
1 CASE

FIG. 77. Ileocolitis: anatomical distribution—such as type

Furthermore the combinations of these two diseases may take place simultaneously (synchronous) or may occur in sequence (metachronous). Thus if ileitis is designated as E and ulcerative colitis as C and granulomatous colitis as G the following variations may occur EC synchronous combined ileocolitis EG synchronous granulomatous ileocolitis E plus C primary ileitis to which ulcerative colitis is later added and C plus E ulcerative colitis that is later complicated by ileitis

PRIMARY

SECONDARY

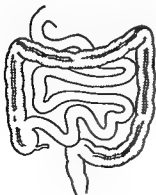


ILEITIS

14 CASES



COLITIS



COLITIS

5 CASES



ILEITIS

FIG 78 Ileocolitis metachronous type

Our present study includes 64 cases of ileocolitis*. Of these 60 represent combinations of true granulomatous ileitis and various forms and distributions of ulcerative colitis. There were 4 cases of granulomatous ileocolitis. In 41 cases both ileitis and ulcerative colitis were present at the onset of the disease so that the combined ileocolitis was synchronous in origin. In 19 cases either ileitis or ulcerative colitis was originally present but after an attempt to cure the original disease by surgical intervention the second disease developed. This group of cases of combined ileocolitis may be called metachronous in nature signifying that the combined diseases succeeded or followed each other. There were 4 cases of granulomatous ileocolitis: one with extensive involvement of the colon including the rectum; one with extensive involvement of the colon excepting the rectum; and two with the granulomatous process localized to the ascending colon only (fig. 17 and 78).

Etiology

The age and sex distribution of ileocolitis is similar to that of the two independent diseases. The age incidence ranged from 9 to 70 years with the average or mean age being 26.5. There were 29 female and 35 males.

The pathologic distribution of the involved segments in ileocolitis are so variable and heterogeneous that an exact classification is impossible. The following table is an attempt to classify the 45 cases of synchronous ileocolitis —

TABLE 20

Terminal ileum and proximal colon	19 cases
Terminal ileum and transverse colon	2
Terminal ileum and whole sigmoidal colon	11
Ileum and jejunum and whole colon	6
Terminal ileum and distal colon	5
Terminal ileum and entire colon including rectum	1
Total	45 cases

It is important to note in the study of the life cycle of cases of segmental colitis that the inflammatory process spread distally from the proximal colon, the process stopping or carrying for long period of time at the sigmoid flexure extending into the rectum rarely only late in the course of an intractable and particularly virulent type of invasion and progression. However the rectum is not immune. In several cases

including two fatal instances that succumbed after multiple and unsuccessful resections the terminal phase was marked by a severe proctitis. In four other living cases it was necessary to resort to ileo tomy as a life saving measure to prevent the patient from succumbing to a severe proctitis with its frequent rectal complications.

Clinical Features

Diarrhea, cramp and fever are the most common symptoms of ileocolitis. Cramps and diarrhea are almost always present. Fever is present during the acute or active phases of the disease ranging from 101° F to 102° F in the low grade cases. In acute toxic cases the temperature may reach as high as 106° F. Leukocytosis with polynucleosis corresponds to the fever with leukocyte counts ranging from 12,000 to 16,000 per cubic millimeter and occasionally reaching 20,000. However counts below 10,000 per cubic millimeter with a high polynucleosis and many young unsegmented polymorphonuclear leukocytes with toxic granulations are frequently found in the acute cases. The sedimentation rate corresponds to the fever and to the leukocytosis but usually remains elevated during the afebrile periods until the inflammation completely subsides. Foul diarrhea with or without bloody stools and cramps is usually present but the tenesmus and rectal urgency found in universal ulcerative colitis are absent. In four cases there was an absence of diarrhea and even constipation was noted. Gross fresh hemorrhage per rectum was present in 11 instances and was massive producing shock in 3 cases. melena was noted twice.

Severe anorexia and progressive weight loss occur during the acute recurrences and in extreme cases losses of 50 to 60 pounds may occur producing severe malnutrition and cachexia. Signs of vitamin B deficiency are especially frequent with glossitis and rhagades being the most frequent. Deficiency of vitamin K causing bleeding due to increased prothrombin time is found in the more intractable cases. An elevated alkaline phosphatase has been noted in several instances in the serum but its significance is not yet understood perhaps this is related to liver damage which in itself may lead to a vitamin K deficiency. Secondary anemia is consistently present with the hemoglobin level ranging between 9 and 11 grams per 100 cc. In the febrile cases with hemoconcentration the hemoglobin values may be normal so that it is important to check them with hematocrit readings. Hypoproteinemia is the rule but is usually mild in the more protracted cases the protein value may drop to 3.2 grams with a marked decrease in the serum albumen causing a reversal

in the albumin globulin ratio. Hypocalcemia and tetany were observed in only 3 cases. Arthritis was present in 18 instances usually involving the larger joints. An associated duodenal ulcer was present in 7 patients and the history of infectious mononucleosis was noted in 3 instances.

An abdominal mass was palpable in 26 instances usually placed in the right lower quadrant. Splenomegaly was noted in 4 instances and clubbing of the fingers was present in 6 cases. Erythema nodosum occurred 17 times in the lower extremities and stomatitis with ulcerative pharyngitis twice. Phlyctenular conjunctivitis was noted once. Intestinal obstruction causing abdominal distention and fluid levels in the small intestine occurs rarely and usually subsides after intestinal intubation.

Internal fistulas originating in the diseased terminal ileum extend



FIG. 79 Granulomatous colitis involving terminal ileum and ascending colon

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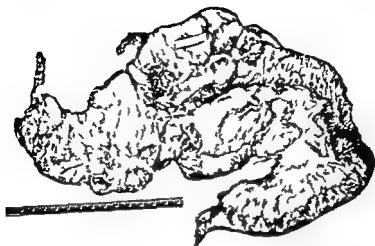


FIG. 81 Combined ileocolitis resected specimen

Medical Therapy

Medical treatment is the first choice and should be attempted in all cases of ileocolitis unless there are definite and well defined indication for surgical intervention. As in the simple cases of ileitis or ulcerative colitis the essential part of the therapy consists of supportive therapy including bed rest, a high protein bland low residue diet, intravenous fluid and plasma or blood whenever necessary to restore normal blood values. We find injections of crude liver extract and vitamin B complex to be very helpful.

The insoluble sulfonamide and antibiotics such as tetracycline and dihydrostreptomycin are used to combat secondary infection. Penicillin is of no value for the treatment of this disease and its complications. However steroid therapy has been of definite value and is especially effective in the acute stages of high fever and intoxication. This is best administered in the form of corticotropin (Acthar) gel parenterally or in the newer long acting zinc corticotropin preparation that need to be administered only once in 48 to 72 hours. Once the desired improvement is obtained the steroid therapy may then be continued with prednisone (Meticorten) or hydrocortisone (Hydrocorten) orally. In many

to the cecum and other parts of the colon in 10 cases and in one instance a jejuno ileal fistula occurred. External fecal fistulas to the anterior abdominal wall complicated 7 cases. Four of these fecal fistulas were secondary to a perforated ulcerative colitis of the sigmoid and 2 fistulas originated in the terminal ileum. Rectal complications were frequent

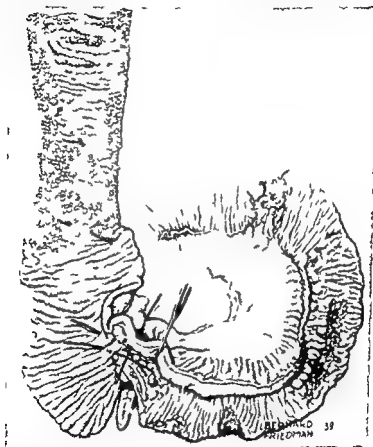


FIG 80 Combined ileocolitis granulomatous ileitis with fistulas and ulcerative colitis with pseudo polypoid

perirectal abscesses and fistula were present in 25 cases. 4 cases were associated with rectovaginal fistulas and in one male there was a deep rectourethral fistulous tract.

he is well and weighs 190 lbs (86 kg). In two cases of terminal ileitis and proctitis an ileotransverse colectomy was performed followed by progression of the colitis with perianal abscesses finally necessitating ileostomy. In 10 cases ileocolic resection and ileosigmoidostomy were performed for terminal ileitis and right-sided colitis. Of these patients 4 required ileostomy after the rectum became involved. 3 patients definitely are improved. 2 are in poor condition due to recurrent disease the last has just been operated on.

One case of terminal ileitis was associated with a granulomatous colitis involving the entire colon including the rectum. Exactly two years prior to the time of writing a total colectomy and resection of the terminal ileum was performed at one stage and the pathologic specimen revealed typical granulomatous ileitis associated with a thickened colon containing giant cell systems and epithelioid tubercles suggesting the diagnosis of granulomatous colitis. The patient made an uneventful recovery and gained 40 lb with a permanent ileostomy.

In two cases a diffuse ileojejunitis was associated with a diffuse ulcerative colitis involving the entire colon excepting the rectum. In one patient an ileosigmoidostomy and subtotal colectomy were performed. He continues in poor nutrition with acute exacerbations of fever and diarrhea due to the residual ileojejunitis. The second patient has been observed for 18 years and presents the life history of ileojejunitis and right-sided colitis with the gradual progression of the disease to involve the entire colon. In this patient the clinical course began with a terminal ileitis and proximal colitis at the age of 20 years. Subsequently he developed a diffuse ileojejunitis with a gradual extension of the colitis to involve the entire colon including the rectum. Over the course of 16 years multiple resections of the small and large intestine were performed and at present he is left with an ileostomy situated 7 feet from the ligament of Treitz. His serum electrolytes and hemoglobin are stabilized at normal levels. His weight is constant and he is returned to working efficiency. A typical granulomatous ileitis was reported by pathologic examination of the specimen. The ascending colon revealed a chronic hyperplastic and polypoid colitis. The remaining part of the transverse and descending colon including the rectum revealed a typical chronic ulcerative colitis (fig. 79).

Metachronous Ileocolitis There were 19 cases of metachronous ileocolitis. Fourteen of these originated as terminal ileitis the ulcerative colitis developing after an ileotransverse colectomy (with or without ileo-

instances results of the oral use of steroids are disappointing because of their poor absorption. One patient with diffuse disease of the small and large intestine made a remarkable recovery, gaining 30 lb (14 kg) and was able to resume his work as a mail carrier after treatment with corticotropin gel daily to prevent the recurrence of his symptoms. Another patient 70 years of age with high temperature, marked intoxication and erythema nodosum of the legs became asymptomatic after six injections of corticotropin.

Of the 18 patients treated medically, one is cured, 2 are well, 5 are improved and 8 continue to have frequent recurrences and are in a chronic state of malnutrition. One patient died at the age of 70 and one patient was lost to follow up. The patient who was cured had a typical terminal ileitis with concurrent involvement of the transverse colon. He was treated with nonspecific protein shock therapy in the form of typhoid vaccine given intravenously. He showed a dramatic response and four years later a x-ray examination revealed a normal mucous membrane throughout the entire colon and a slight distortion of the terminal ileum. 18 years after the original illness the man is well.

Surgical Management

In this series 46 patients were treated surgically, multiple operations being required in most instances. The surgical approach to the treatment of ileocolitis presents numerous and complex problems even to the most experienced surgeon. In general surgical intervention is most successful where the disease is localized to the distal part of the ileum and proximal part of the colon and the patient has not responded to medical therapy. Local palliative resections of stenotic diseased areas of ileitis and jejunitis are frequently necessary when intestinal obstruction exists. Occasionally massive resections of the colon and small intestine have been necessary because of exanguinating hemorrhage or progressive disease.

Synchronous Ileocolitis. There were 27 cases of synchronous ileocolitis treated surgically. In 14 of these cases the disease was limited to the terminal ileum and ascending colon. Ileocolic resection was performed in 11 and a short circuiting procedure (ileotransverse colectomy) in the other 3 instances. Results were good in 7 cases, poor in 6 due to recurrent disease, one patient died after a secondary resection.

In the remaining 13 cases one patient had an ileoigmoidotomy with resection of the ileum for terminal ileitis and transverse colitis.

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In the remaining 13 cases one patient had an ileosigmoidostomy with transection of the ileum for terminal ileitis and transverse colitis.

omatous ileitis proximal to the ileosigmoidostomy 46 cm of terminal ileum was resected and granulomatous ileitis with fistula formation was revealed. She had a normal full term pregnancy three years ago however during the eighth month of her second pregnancy she had a recurrence of fever and diarrhea and at the time of cesarean section ten months ago acute ileitis was seen proximal to the site of the anastomosis. Because of recurrent intestinal obstruction 18 inches of granulomatous ileitis was resected three months ago. The patient now weighs 115 lb has only three to four stool a day and is an active housewife despite the presence of a high ileosigmoidostomy.

The fifth patient with a subtotal colectomy and ileosigmoidostomy for right sided ulcerative colitis developed proctitis requiring ileostomy. At this time a segment of granulomatous jejunitis 18 inches in extent was resected. Six years later she developed granulomatous ileitis involving the terminal 24 inches of ileum immediately proximal to the site of the ileostomy. Both the jejunitis and the ileitis were typically granulomatous containing skip lesions and did not resemble the superficial ulcerative ileitis frequently seen after ileostomy. This ulcerative ileitis is prone to occur when there is stenosis of the ileostomy tooma causing obstruction. This complication has occurred 5 times in our experience. In addition we have had 2 patients in whom ileostomy was performed who developed soon thereafter a severe necrotizing diffuse ileojejunitis with a fulminating clinical course complicated by massive hemorrhage and with a fatal outcome within 48 hours.

Prognosis and Results

Of the 18 patients treated medically 3 are well and 5 are improved but 8 are in poor condition with frequent recurrences. One patient died and one patient was lost to follow up. Results in the 46 surgical cases can be considered good in only 12 patients. 8 improved, 21 are poor, 2 died and 3 patients are lost to follow up. Fourteen of these surgical patients eventually required permanent ileostomy. As expected the prognosis in the combination of the two severe inflammatory diseases is poor. When the disease remains localized to the terminal ileum and small adjacent segments of the colon the results are generally good. Many of the 11 patients in our series had complicated cases and had been referred to our office after previous unsuccessful attempt at medical or surgical cure.

After 25 years of experience in handling these complicated cases

colic resection) had been performed. In one case the secondary colitis was restricted to the transverse colon and after a subsequent resection the patient was well. A second patient after a short circuiting procedure for terminal ileitis developed diffuse ulcerative colitis but his disease has been in a continuous remission for the past five years. Two other patients after an ileocolic resection for ileitis developed a mild but persistent ulcerative colitis. In another case death followed infection with clostridia; one patient was lost to follow up. The remaining 8 patients who originally had terminal ileitis developed a subsequent ulcerative colitis after surgical intervention for the cure of the ileitis. In all 8 patients the subsequent ulcerative colitis has been severe requiring ileostomy in three instances. One of the latter cases began with a terminal ileitis when the patient was 28 years of age. After an ileotransverse colostomy and subsequent ileocolic resection including 4 feet of diseased terminal ileum there was marked improvement for seven years. He then developed increased diarrhea associated with chills and fever. Barium enema three years ago revealed ulcerative colitis involving the sigmoid and lower part of the descending colon. Despite intensive treatment including steroid therapy his course was downhill and resection of the entire distal part of the colon including the rectum was required for severe advanced ulcerative colitis causing massive hemorrhage. At present the ileostomy drainage averages 3 liters but the patient's weight is stabilized at 130 lb (59 kg) and his blood electrolytes are within normal range without intravenously given supplements.

The other 5 cases of metachronous ileocolitis began with right sided ulcerative colitis for which subtotal colectomy with ileosigmoidostomy was performed. In 2 of the 5 cases the resected terminal ileum was normal; the other 3 cases presented the typical backwash ileitis. Within five years a true granulomatous ileitis developed in 4 of these patients in the new terminal ileum proximal to the site of the ileosigmoidostomy. Of the 4 patients 2 required subsequent ileostomy due to rectal complications and are well now. A third patient developed mild proctitis and duodenal ulcer. The fourth case is significant because granulomatous ileitis recurred twice after resection for right sided ulcerative colitis and yet the sigmoid and rectum are still perfectly normal. This patient is now 28 years of age; at the age of 18 she underwent a subtotal colectomy and ileosigmoidostomy for right sided ulcerative colitis with a fecal fistula to the abdominal wall. Five years later she developed recurrent symptoms and radiographic studies revealed a typical granu-

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- 4 Albright F and Stewart J D Hypothesis of all fat soluble vitamins due to steatorrhea *New England J Med* 223 239 41 1940
- 5 Althausen T L Uyeyama K. and Simpson R G Digestion and absorption after massive resection of the small intestine Presented at the annual meeting Am Gastroenterological Assoc April 30 1948 at Atlantic City N J
- 6 Anderson D O Mullinger ■ A and Bogoch A Regional enteritis involving the duodenum with clubbing of the finger and steatorrhea *Gastroenterology* 32 917 926 1957
- 7 Anschütz G Ueber unpezifische entzündliche Geschwulste des Dickdarms *Deutsch Zsch Chir* 243 377 1934
- 8 Arnheim ■ Regional ileitis with perforating abscess and peritonitis *J Mt Sinai Hosp* 2 61 1935
- 9 Ascencio Camacho F Regional enteritis: Puerto Rico *Gastroenterology* 6 483 1946
- 10 Ashley L B Meyers S G and Reynold L Regional enterocolitis *J Michigan State M Soc* 42 109 1943
- 11 Ave y Jones F and Pailey J W Intestinal hypodystrophy *Lancet* 1 214 940
- 12 Babson W W Terminal ileitis with obstruction and abscess complicating pregnancy *New England J Med* 235 544 547 1946
- 13 Barbou R F and Stokes A B Chronic cicatrizing enteritis A phase of benign nonspecific granuloma of the small intestine *Lancet* 1 299 303 1936
- 14 Baigen J A Regional enteritis problem in management *Wisconsin M J* 54 367 1955
- 15 Bargen J A Wesson H R and Jackman R G Studies in the ileocecal valve (ileocecu) *Surg Gynec & Obst* 11 31 1940
- 16 Barker W H and Hummel L E Macrocystic anemia in association with terminal strictures and anastomoses Review of literature and report of two new cases *Bull Johns Hopkins Hosp* 64 215 256 1939
- 17 Bell H G Chronic catarrhing enteritis California and West Med 41 239 1934
- 18 Berman J K Brown H M Foster R T and Gitsell T L Massive resection of the intestine *J A M A* 135 918 919 1947
- 19 Bernstein M Konikman F W and Scllick D M Beck & Co'd Report of a case with visceral involvement *Arch Int Med* 44 721 1929
- 20 Binnys H Discussion of paper by C G Miller Regional ileitis *Ann ■ ■* 107 689 1935
- 21 Bgard J D and Henke J A Regional ileitis *J A M A* 108 550 1937
- 22 Bell A D Localized chronic ulcerative ileitis *Ann Surg* 99 957 966 1934
- 23 Blackburn G Hadfield G and Huett A H Regional ileitis *St Barth Hosp Rep* 72 181 24 1939
- 24 Blumenthal J S and Beaman R Terminal ileitis with extension to

of combined ileocolitis one learns the value of a conservative medical approach. Expectant therapy should be the treatment of choice unless there are urgent surgical indications such as recurrent massive hemorrhage, recurrent bouts of intestinal obstruction or persistent fistulas. We have found steroid therapy, especially in the form of corticotropin injection, of definite value in causing remissions and maintaining sustained improvement. The best surgical results in our series were obtained when the patients had been observed for a long period of time and the disease remained localized to the distal part of the ileum and proximal part of the colon. Recurrences have followed invariably when the patient was operated on during the diffuse stages and the surgeon was unable to delimit the segments of involved disease. In the presence of diffuse disease, multiple resections of localized segments causing active symptoms will often bring about marked remission and slowly enable the remainder of the intestine to take over the absorptive function. However, in some instances massive resections of the small and large intestine may be necessary; these are now possible with satisfactory results after preoperative preparation with multiple transfusions and antibiotics.

In these confusing, complicated, often bewildering forms of combined disease (ileitis and colitis or ileocolitis) no absolute rule can be laid down for the approach to surgical therapy. Every case must be considered on an individual basis since there are so many variant and so many possible combinations of the different factors. Where medical therapy fails, where fistula formations, abdominal masses, perirectal abscesses and fistulae persist, where gross massive hemorrhage or obstruction of the small intestine supervenes, one has no choice but to ask for radical surgical interference. And this in face of the fact that radical surgical intervention seems to offer little but amelioration and is so often followed by disappointing recurrences or by spread of the disease to new anatomic territories. Medical cures or permanent cures under conservative therapy are very few.

References

1. Abercrombie, J. *Pathological and Practical Researches on Disease of the Stomach, the Intestinal Tract and Other Viscera of the Abdomen*. Edinburgh: W. & J. G. Baillière, 1828, p. 238.
2. Adlersberg, H., and Sobotka, H. Fat and vitamin A absorption in true and jejuno ileitis. *Gastroenterology* 7: 357, 1943.
3. ——— and Weingarten, M. Enteropathy in deficiency state. *New York State J. Med.* 41: 1418, 1941.

- 47 Carlisle J C and Judd E S Regional enteritis involving the duodenum
Proc Staff Meet Mayo Clinic 7: 569 1952
- 48 Camiel M R Iliocolic tube culosis Radiology 44: 344-351 1945
- 49 Caeten D Nutritional disturbance in regional enteritis Surg 6: 703-716 1939
- 50 Cave H W Inflammatory lesions of the small intestine Surgical aspects
J A M A 127: 456 1945
- 51 Chesley S Chesley D, Olander G Bennett W, and Cole W H Production
of chronic enteritis and other systemic lesions by the ingestion of
finely divided foreign material Surgery 2: 1-34 1950
- 52 ——— Olander E B Stow C B et al Regional enteritis clinical and
experimental observations Surg Gyn & Obst 91: 343 1950
- 53 Clark E, and Wright A Acute phlegmonous enteritis Arch. Surg
34: 997 1937
- 54 Clark R L Jr and Dixon C F Regional enteritis Surgery 5: 277-304 1939
- 55 Clute H M Regional ileitis A report of two cases Ill Clin North
America 13: 561-567 1933
- 56 Coffey T H Non-specific granuloma causing intestinal obstruction
J A M A 85: 1303 1925
- 57 Cohen H and Fishman A P Regional enteritis and amyloidosis Ga-
stroenterology 12: 100 1949
- 58 Coleman E P and Bennett D A Massive intestinal resection Am J
Surg 59: 429-433 1943
- 59 ——— and ——— Fecal fistulas following acute appendicitis Ann Surg
84: 837 1926
- 60 Colp R A case of non-specific granuloma of the terminal ileum and
the cecum S Clin North America 14: 443-449 1934
- 61 ——— Non-specific granulomata of the intestine Ann Surg 107: 74-81
1938
- 62 ——— Gallock J H and Ginzburg H Ileocolostomy with exclusion
for non-specific ileitis Am J Dig Dis 9: 64-68 1942
- 63 ——— and Ginzburg L Ileocolostomy with exclusion in the treatment
of regional ileitis New York State J Med 41: 98-99 1941
- 64 Comb C and Saunders W A singular case of tracture and thickening
of the ileum Med Tr Roy Coll Phys Lond 4: 16-21 1813
- 65 Conforti M W Weber H M Bagenstoss A H and Kelly W F Non-
specific granulomatous inflammation of the stomach and duodenum A
J M Sc 270: 616 1950
- 66 Connell F G Regional ileitis Am J Dig Dis & Nutrition 3: 438 1936
- 67 Cook W T Nutritional and metabolic factors in the etiology and
treatment of regional ileitis Ann Royal Coll Surg England 17: 137
1935
- 68 ——— and Blake H Non-specific terocolitis Brit J Med 24:
1-22 1953
- 69 Corr P and Boeck W C Chronic ulcerative enteritis Am J Dig Dis
& Nutrition 1: 161-163 1934-35

cecum following non perforating abdominal trauma Minnesota Med
22 406 1939

- 25 Bockus H L Gastroenterology Philadelphia W B Saunders Co
1944 vol 2
- 26 — Present status of chronic regional or cicatrizing enteritis J A M A
171 449 456 1945
- 27 — Johnson T A and Lee W B An appraisal of the results of
surgically treated regional ileitis Lahey Birthday Volume Springfield
Ill C C Thomas 1940 pp 53 83
- 28 — and Lee W E Regional (terminal) ileitis Ann Surg 102 412
421 1935
- 29 Bonorino-Udaondo C Ileitis regionales Prensa Med Argent 27 1141
1151 1940
- 30 — and Castex M R Ileitis regional y trofismo oseo Prensa Med
Argent 34 1523 1947
- 31 — and Centono A M El pronostico en las enteritis segmentarias
Prensa Med Argent 30 774 775 1943
- 32 — Maisa P A and D Alotto V El diagnostico radiologico de los
ileitis segmentarias Prensa Med Argent 27 2011 2107 1940
- 33 Bopp W C Barger J A and Dixon C F Regional enteritis roentgen
therapy Proc Staff Meet Mayo Clinic 25 14 1950
- 34 Bowen W H and Day T H Post mortem in a case of regional ileitis
nine years after symptomatic recovery following ileo colostomy Guy's
Hosp Reports 89 70 76 1939
- 35 Brahdly L and Kahn S Trauma and Internal Disease Philadelphia
Lea & Febiger 1941
- 36 Braun H Ueber Entzündliche Geschwulste des Netzes Arch Klin Chir
63 378 1901
- 37 Brewster H N Personal communication Gastroenterology 1 353 1943
- 38 Brooke B N and Cooke W T Ulcerative colitis diagnostic problem
and the apertic warning Lancet 2 464 464 1951
- 39 Brown P W Barger J A and Weber N M Chronic inflammatory
lesions of the small intestine (regional enteritis) Am J Dig Dis &
Nutrition 1 4 6 431 1934 35
- 40 — and Donald C J J Prognosis of regional enteritis Am J Dig
Dis 9 87 91 1942
- 41 — and Pemberton J de J Solitary ulcer of the ileum and ulcer of
Meckel's diverticulum Proc Staff Meet Mayo Clinic 11 259 1936
- 42 — and Schieffley C H Chronic regional enteritis occurring in three
siblings Am J Dig 6 57 1939
- 43 Brown E Chronic non specific regional enteritis Am J Surg 54 487
495 1945
- 44 Browne H C and McHardy C Primary lesion of jejunum J A M A
115 2257 1940
- 45 Buckstein J Primary ulcer of the jejunum Radiology 33 799 804 1939
- 46 Butt H R and Watkins C H Occurrence of macrocytic anemia in a so-
ciation with lesions of the bowel Ann Int Med 10 222 1936

- 94 Dashiell G H, Karner J B, Klotz A B and Pimer W L. Regional enteritis: a follow up study of forty cases. *Med. Clin. North America* 35: 27, 1951.
- 95 Davis D R., Dockerty M B. and Mayo C W. The myenteric plexus in regional enteritis: a study of the number of ganglion cells in the ileum in 24 cases. *Surg., Gyn. & Obst.* 101: 703-16, 1955.
- 96 Dennis C, Eddy F D. and Weisberger H. Vagotomy in the treatment of idiopathic ulcerative colitis and regional enteritis. *Minnesota Med.* 37: 253, 1948.
- 97 Dixon C F. Regional enteritis. *Ann. Surg.* 103: 857-866, 1938.
- 98 Dowdle E. Multiple primary non-specific jejunal ulcers with chronic duodenal dilatation. *Ann. Surg.* 116: 348, 1942.
- 99 Dreiling, D A. Studies in pancreatic function. *Gastroenterology* 24: 340, 1953.
- 99 Dwyer W L., Hyde P J. and Rhoads J E. Late results in the surgical treatment of regional enteritis. *Pennsylvania M. J.* 57: 433-438, 1954.
- 100 Ebrill D. A case of regional ileitis in childhood. *Brit. J. Surg.* 3: 312-314, 1945.
- 101 Egger C. Discussion of Crohn's. *Ann. Surg.* 9: 132, 1933.
- 102 Elston E. L., and Johnson J. Acute Regional Enteritis. *Int. Clin. N. S.* 1: 123-133, 1940.
- 103 Elman R., and Read J A. Nutritional recovery following removal of all but the first of jejunum and half of the colon. *J. Missouri M. A.* 47: 145-146, 1945.
- 104 Erb L. H. and Farmer A W. Ileocolitis. *Surg. Gynec. & Obst.* 61: 614, 1935.
- 105 Erdmann J. J. and Burt, C. V. Non-specific granuloma of the gastrointestinal tract. *Surg. Gyn. & Obst.* 57: 71-80, 1933.
- 106 Eskine E. H. The pathologic relationship of the enteric adenitis illitis and appendicitis. *Am. J. Clin. Path.* 11: 706-714, 1941.
- 107 Faber K. Pernicious Anemia as a Folge af tarmlidelse. *Hospital Tidende* 601: 1895. *Fests. Roesk.* Band 111.
- 108 ———. Perniciose anemie bei dunndarm tracturen. *Berl. Klin. Wchnsch.* 33: 643-646, 1897.
- 109 Fallis L. S. Massive antitestinal hemorrhage in regional ileitis. *A. J. Surg.* 53: 512, 1941.
- 110 Felger L. and Schenk H. L. Recurrence in sigmoidal enteritis following radical resection. *A. J. Surg.* 49: 307-315, 1940.
- 111 Felton J. Non-specific ulcerative colitis: terminal (distal) ileitis and bacillary dysentery. The common pathogenesis. *New York State J. Med.* 35: 576-578, 1935.
- 112 ———. The relationship of bacillary dysentery to distal ileitis, chronic ulcerative colitis and non-specific intestinal granuloma. *Ann. Int. Med.* 10: 645-669, 1936.
- 113 Frost E. Hemorrhagic ulcerosa. *Bun. Best.* 161: 46, 1936.

- 70 Copwell H B Massive resection of small intestine *Ann Surg* 127 377 1948
- 71 Coutts W E and Opozol L Lymphogranulomatosis of mouth small and large bowel rectum and anus *Rev Chil Hyg y Med* 2 35 1939
- 72 Crane A W A roentgenologic sign of mucous colitis *Am J Roentg and Rad Rev* 17 416 1917
- 73 Crockett R W Psychiatric findings in Crohn's disease *Lancet* 1 946 1952
- 74 Crohn B B Indications for surgical intervention in regional ileitis *Arch Surg* 74 305 311 1957
- 74a — The broadening conception of regional ileitis *A J Dig Dis & Nutrition* 1 97 99 1934 35
- 75 — Regional ileitis *Surg Gynec & Obst* 68 314 321 1939
- 76 — Editorial Acute appendicitis and diarrhea *Gastroenterology* 4 511 1945
- 77 — Clinical use of sulfasuxidine *Gastroenterology* 1 140 146 1943
- 78 — The use of sulfonamides in ileitis *Gastroenterology* 4 11 13 1945
- 79 — The relationship of trauma to diseases of the gastrointestinal tract *Gastroenterology* 8 735 742 1947
- 80 — Trauma and Disease *In* Brahdry and Kahn Philadelphia Lea & Febiger 1941 p 185
- 81 — Benign diseases of the small intestine *Gastroenterology* 2 383 394 1944
- 82 — and Berg A A Right sided (regional) colitis *J A M A* 110 32 38 1938
- 83 — Garlock J H and Yarnis H Right sided (regional) colitis *J A M A* 134 334 338 1947
- 84 — Ginzburg L and Oppenheimer G D Regional ileitis A pathologic and clinical entity *J A M A* 99 1323 1932
- 85 — and Janowitz H B Reflections on regional ileitis twenty years later *J A M A* 156 221 1954
- 86 — and Rosenak B D A combined form of ileitis and colitis *J A M A* 106 1 7 1936
- 87 — and Yarnis H The anatomical position of the ileum in health and disease *Radiology* 33 325 330 1939
- 88 — and — Continuous fever of unknown origin *Ann Int Med* 26 858 1947
- 89 — Yarnis H and Koelitz B Regional ileitis complicating pregnancy *Gastroenterology* 31 615 1956
- 90 — and Yunich A M Ileocejunitis *Ann Surg* 113 371 380 1941
- 91 Cutler E C A neglected entity in abdominal pain and a common disease Cicatricial enteritis *New York State J Med* 39 328 1939
- 92 Cushway B C Chronic cicatrizing enteritis Regional ileitis (Crohn) *Illinois M J* 66 525 1934
- 93 Dalziel T K Chronic interstitial enteritis *Brit M J* 2 1068 1070 1913

- 136 Gorre M. Massive intestinal resection. *ML Surg* 103: 3, 1943
- 137 Gray S T, Reisfentsein R W., Benson J A Jr and Gordon Young J C. Treatment of ulcerative colitis and regional enteritis with ACTH. *Arch Int. Med* 87: 646-66, 1951
- 138 Green R. B. Chronic non-specific jejunitis. *U S Naval Bull* 49: 482, 1949
- 139 Hoen J and Pompen A. W. M. Het regionale Geneeskundige Bladen Haarlem, de eerste F. Bohn. N. V., 1935
- 140 von Haber H. Unspezifische Entzündung des Ileokolons. *Muench Med Wchnsch* 81: 479-483, 1934
- 141 Hadfield G. The primary histologic lesion of regional ileitis. *Lancet* 2: 773-775, 1939
- 142 Halligan E. J. and Halligan H. J. Acute free perforation at fistula of regional enteritis. *Am J Surg* 70: 493-497, 1937
- 143 Halloway J W. Regional ileitis. *Ann Surg* 118: 379, 1943
- 144 Harris F I. The earliest acute stage of regional enteritis. Report of case in a child. *Arch Pediat* 57: 367-376, 1940
- 145 ——— Bell G H and Brunn H. Chronic catarrh of enteritis. Regional Ileitis (Crohn). A new organic entity. *Surg Gynec & Obst* 57: 637, 1933
- 146 Hertzberg J. Jejunitis acuta. Oslo. Blicher & Larén, 1954
- 147 Hirsch E F. Relation of the chemical composition of the lipid to character of tissue lesion. *Arch Path* 71: 316, 1941
- 148 Holm C E. The fate of the side tracked loop of ileum following lateral anastomosis for complete benign obstruction. *Surg Gynec. & Obst* 56: 746, 1933
- 149 Holman C C. Survival after removal of twenty feet of intestine. *Lancet* 2: 597, 1944
- 150 Homsen I and Hils G M. Regional ileitis. A clinical, not a pathological entity. *New England J Med* 209: 1315-1324, 1933
- 151 Horn R. C. Jr., and Rhoads J M. Regional enteritis involving Meckel diverticulum perforation of the diverticulum and fistula formation. *Ann Surg* 119: 274-278, 1944
- 152 Hurst A F. Regional ileitis (Crohn's disease). I and II. *Gy's Hosp Rep* 89: 54-70, 1939
- 153 ———. A case of Addison's anemia with subacute combined degeneration of the spinal cord and normal gastric secretion following chronic obstruction of the ileum. *Gy's Hosp Rep* 87: 175, 1937
- 154 Huebner O W. Roentgen diagnosis of jejunitis acuta phlegmonosa. *Acta Radiolog* 29: 71, 1948
- 155 ———. Case of chronic non-specific jejunitis and distensions. *Acta Radiolog* 29: 516-518, 1948
- 156 Ingling F J. The progress of benign intestinal conditions. Read at the 51st Annual Meeting of the Association of Life Insurance Medical Directors of America. Oct. 11-12, 1951
- 157 Jackman R J. Anal abscess and anal fistula in association with regional ileitis. Report of case. *Proc Staff Meet. Mayo Clinic* 18: 154-156, 1943

- 114 Fermin N G and Amieba R F Enteritis regional Arch Med de San Lorenzo 2 351 1951
- 115 Fick K A and Wolken A B Necrotic jejunitis Lancet 1 519 1949
- 116 Fischer A Appendicitis und granulomata Ztschr f Chir 58 1243 1931
- 117 Fischer A W and Lurmann Ueber eine tumorbildende ulcerose stenosierende und perforierende entzuendung des unteren ileum Arch fur Klin Chir 177 638 650 1933
- 118 Forbes R B and Duncan J Some observations on regional ileitis and allied conditions West J Surg Obst & Gynec 43 362 367 1937
- 119 Frazer A C Fat metabolism and the sprue syndrome Brit M J 2 769 1949
- 120 Frazer I and Haggart H Crohn's disease J Royal Army Med Corps 84 9 13 1945
- 121 Friedl Meyer M kasuistischer Beitrag zur tumorbildenden ulcerosen stenosierenden Entzuendung des unteren ileum (Ileitis terminalis) Schweiz Med Wchnschr 66 503 512 1936
- 122 Galambos A and Mittleman W Typical and atypical terminal ileitis Am J Dig Dis & Nutr 2 442-447 1935 16
- 123 Garlock J H Present status of regional ileitis Am J Surg 12 875 1946
- 124 — and Crohn B B An appraisal of the results of surgery in the treatment of regional ileitis J A M A 124 205 208 1945
- 125 Gendel S and Beaver M C An unusual case of Meckel's diverticulum Ann Surg 121 981 983 1945
- 126 Ginzburg L Persistent abdominal fecal fistulas due to regional ileitis Surgery 7 515 523 1940
- 127 — Colp B and Sussman M Ileocolostomy with exclusion Ann Surg 110 643 655 1939
- 128 — and Garlock J H Regional ileitis Ann Surg 116 906 912 1942
- 129 — and Oppenheimer C D Non specific granulomata of the intestines (inflammatory tumors and stricture of the bowel) Ann Surg 98 1046 1933
- 130 Gisbe tz H Ist die Radikale Operation der unpezifischen umschriebenen Entzuendung de Ileumendes notwendig? Zentr Chir 63 2687 1936
- 131 Golden A Primary systemic amyloidosis of the alimentary tract Arch Int Med 75 413 416 1945
- 132 Goldstein H I The history of regional ileit Essays on history of medicine Victor Robin on Memorial Volume ed Kagan New York Froben 1948
- 133 — The history of regional ileitis Schweiz Med Wchnschr 33 1035 1950
- 134 Goldfarb S J The roentgen diagnosis of lesion of the small intestine New York State J Med 34 500 505 1934
- 135 Golob M Infectious granuloma of the intestine with special reference to the difficulty of pre operative differential diagnosis M J & Rec 135 390 1932

- 136 Gorse M. Massive intestinal resection. *Mil Surg* 103: 282, 1948.
- 137 Crav S. T. Reifent ein. W. Benson J. A. Jr. and Gordon Young J. C. Treatment of ulcerative colitis and regional enteritis with ACTH. *Arch Int Med* 87: 646-667, 1951.
- 138 Genn R. B. Chronic nonspecific jejunitis. *U S Naval Bull* 49: 458, 1949.
- 139 Groen J. and Pompen A. W. M. Ileitis regionalis. *Geneeskundige Bladen Haarlem de e ren F B hu* 11: 1935.
- 140 von Haberer H. Unspezifische Entzündung des Ileozökums. *Muench Med Wchnchr* 81: 479-483, 1934.
- 141 Hadfield G. The primary histological lesion of regional ileitis. *Lancet* 2: 773-775, 1939.
- 142 Halligan E. J. and Halligan H. J. Acute free perforation as first sign of regional enteritis. *Am J Surg* 31: 493-497, 1937.
- 143 Hallway J. W. Regional ileitis. *Ann Surg* 118: 329, 1943.
- 144 Harter F. I. The earliest acute stage of regional enteritis. Report of case in a child. *Arch Pediat* 57: 367-376, 1940.
- 145 ——— Bell G. H. and Brun H. Chronic crusting enteritis. Regional ileitis (Crohn). A new surgical entity. *Surg Gynec & Obst* 51: 637, 1933.
- 146 Hertzberg J. Jejunitis acuta. Oslo. Bohler & Larsen, 1954.
- 147 Hirsch E. F. Relation of the chemical composition of the lipid to character of the tissues. *Arch Path* 31: 516, 1941.
- 148 Holm C. The fate of the de-tracked loop of ileum following lateral anastomosis for complete benign obstruction. *Surg Gynec & Obst* 56: 746, 1933.
- 149 Hildman C. C. Survival after removal of twenty feet of intestine. *Lancet* 2: 597, 1944.
- 150 Honan I. and Hass C. M. Regional ileitis. A clinical not a pathological entity. *New England J Med* 209: 1315-1324, 1953.
- 151 Horn R. C. Jr. and Rhoads J. M. Regional enteritis involving Meckel's diverticulum: perforation of the diverticulum and fistula formation. *Ann Surg* 119: 74-78, 1944.
- 152 Hurst A. F. Regional ileitis (Crohn's disease). I and II. *Guy's Hosp Rep* 89: 54-70, 1939.
- 153 ——— A case of Addison's anemia with subacute combined degeneration of the spinal cord and normal gastric secretion following chronic obstruction of the ileum. *Guy's Hosp Rep* 81: 175, 1937.
- 154 Huchoy O. W. On roentgen diagnosis of jejunitis acuta phlegmonosa. *Acta Radiologica* 29: 71, 1943.
- 155 ——— Case of chronic specific jejunitis and steatorrhea. *Acta Radiologica* 29: 516-518, 1943.
- 156 Ingelfinger F. J. The prognosis of benign intestinal obstruction. *Read at the Sixtieth Annual Meeting of the Association of Life Insurance Medical Directors of America*, Oct. 11-13, 1951.
- 157 Jackman R. J. An ileocecal and anal fistula in association with regional ileitis. Report of case. *Proc Staff Meeting Mayo Clinic* 18: 154-156, 1943.

- 158 — and Bue L A Tuberculosis and anal fistula *J A M A* 130 630 632 1946
- 159 — and Smith N D Some manifestations of regional ileitis observed sigmoidoscopically *Surg Gynec & Obst* 76 444 1943
- 160 Jackman W A Localized hypertrophic enteritis as a cause of intestinal obstruction with a report of two cases *Brit J Surg* 22 27 32 1934
- 161 Jackson A S Regional enteritis *Surg Gynec & Obst* 65 1 10 1937
- 162 James W L Regional jejunitis *Radiology* 50 532 534 1948
- 164 Jellen J Regional ileitis A review of fifty cases *Am J Roentg and Rad* 37 190 201 1937
- 165 Johnson W R Chronic non specific jejunitis with unusual features *Gastroenterology* 1 346 1943
- 166 Kantor J L Regional (terminal) ileitis Its roentgen diagnosis *J A M A* 103 2016 2021 1934
- 167 Kawel C A Jr and Tesluk H Brunner type glands in regional enteritis *Gastroenterology* 28 810 820 1955
- 168 Kazmann H A and Barnett L A Non specific regional jejunitis Review of *Gastroenterology* 18 605 607 1951
- 169 Kemp C E Perlintero J and Wein W Cicatrizing enterocolitis in a newborn infant *A J M Sc* 214 23 33 1947
- 170 Kibaya A K Possible case of Crohn's disease in a Ruando native East African *M J* 23 317 1946
- 171 Kiefer E D The diagnosis of regional ileitis (chronic idiopathic ulcerative enteritis) *Surg Clin North America* 23 862 872 1943
- 172 — Recurrent regional ileitis *Lahey Clin Bull* 8 149 1953
- 173 — and Ross J R Criteria in the management of chronic ileitis *J A M A* 179 104 108 1945
- 174 Killian S T and Ingelfinger F J Nutritional problems presented by patient with extensive jejuno ileitis *Arch Int Med* 73 466 1944
- 175 Kirklin B ■ Discussion of a paper by Brown P W *Am J Roentgen* 54 496 1945
- 176 Kirsner J B Owens F M and Humphreys E M Regional enteritis in father and son *Gastroenterology* 10 883 891 1948
- 177 Koenig A S Jr Chronic jejunitis *Arch Path* 40 187 190 1945
- 178 Koletsky ■ and Strecher R M Primary systemic amyloidosis *Arch Path* 27 267 283 1939
- 179 Konieczny G E Discussion *Zentr Chir* 59 2534 1932
- 180 Korte W Ueber entzündliche Geschwulste am Darm *Arch Klin Chir* 118 138 1921
- 181 Koster H Kayman L P and Sheinfeld W Regional ileitis *Arch Surg* 37 789 1936
- 182 Kross I Terminal ileitis Conservative surgical treatment *Am J Dig Dis & Nutr* 5 313 314 1938 39
- 183 Ladd W ■ Quoted by Homans and Haas *New England J Med* 209 1323 1933

- 184 Lahey F H and Sanderson E Lesions of the right colon involving right colectomy J A M A 120 1356 1942
- 185 Lando F Zirkumskripte Enteritis am Dickdarm Zentr Chir 50 816 1921
- 186 — Ueber Ileitis Ulcerosa Zentr f Chir 64 1690 1937
- 187 Lehman E P Regional enteritis The acute phase Rev Gastroenterology 6 222 1939
- 188 Lentweitz J and Rothfeld J Diffuse Nodular sarcoid Arch Derm Syph 161 504 1930
- 189 Lewohn R Segmental enteritis Surg Gynec & Obst 66 215 222 1938
- 190 — and Colp R In Prognosis Regional Ileitis Cohn H B Am J Dig Dis & Nutrition 3 733 1936
- 191 Likely D S and Liza J R Chronic granuloma Am J Dig Dis 6 113 1939
- 192 Lombardi A and Maneru J Su la localisation de la maladie de Nicolas Faveur au l'intestin grêle stenosis leala multiples Ann d Anat Path 16 597 1939
- 193 Longcope W T and Pierson J W Boeck's sarcoid (sarcoidosis) Bill John H skin Hosp 60 223 296 1937
- 194 Lobb S H Shay H and Woloshin H A roentgen study of the gastrointestinal tract: proven case of sarcoidosis review of the literature Gastroenterology 6 451 1954
- 195 Lowen A Ub Appendicitis Fibroplastica Deutsch Ztsch f Chir 129 221 241 1934
- 196 Luft F J Roentgenological studies of the mucosa of the terminal ileum Am J Roentg and Rad 45 63 68 1941
- 197 Lyall A Regional ileitis Glasgow M J 143 10 1945
- 198 Lyons A S and Glick J H Localized perimal jejunitis Arch Surg 53 702 704 1946
- 199 McGuff P McKerty M B Wagh J M and Randall L M Endometritis as a cause of intestinal obstruction Surg Gynec & Obst 86 273 1948
- 200 McLe C E Cecinidism of the ileum Am J Clin Path 14 310 1944
- 201 McKinnon D C Spontaneous cure of a fulminating regional enteritis M J Med 77 744-746 1939
- 202 McKee T T V tam dehiscence and the small intestine J A M A 117 910 1941
- 203 — and Pind R E Changes in the gastrointestinal tract in deficiency states J A M A 104 313 316 1935
- 204 Mal R A te gonolitis A report of two cases with bacteriologic findings Br J Surg 25 517 1937
- 205 Miller B The Principles of Pathological Histology Philadelphia Saunders 1914
- 206 Merrill F Regillier New England J Med 375 382 1940

- 207 ——— Regional ileitis Surgical management and results of operation
S Clin North America 23 873 880 1943
- 208 ——— and Mathieson W L Surgical treatment of chronic regional
enteritis Lahey Clin Bull 2 66 71 1955
- 209 Martin F R R and Carr R J Crohn's disease involving the stomach
Brit Med J 1 700 1953
- 210 Mayo C W and Judd E S Surgical resection in non specific ileo
colitis J A M A 111 836 1941
- 211 Meade H H Jr Acute segmental enteritis Pennsylvania M J 44
1519 1526 1940 41
- 212 Megret R Ileite terminal aigue primitive chez un enfant de trois ans
Mem Acad de Chir 65 380 387 1939
- 213 Meulengracht E Pernicious anemia in intestinal strictures Acta Med
Scand 72 231 240 1929
- 214 Meyer K A and Rosi P A Regional enteritis (non specific) N Clin
North America 15 697 711 1935
- 215 Mixter C C Regional ileitis Ann Surg 107 674 694 1935
- 216 Mock H E Infective granuloma Surg Gynec & Obst 57 672 689 1931
- 217 Molesworth H W L Granuloma of intestine Stenosis of ileocecal valve
Brit J Surg 21 370 372 1933 34
- 218 Monks G H Studies of surgical anatomy of the small intestine and its
localization Ann Surg 47 543 569 1904
- 219 Morehead R P Regional enteritis with observations concerning patho
genesis North Carolina M J 8 216 1947
- 220 Morgagni J B The Seats and Causes of Disease Investigations by
Anatomy London 1769 vol 2 p 75 Also de Sedibus et Causis Mor
borum Venice 1761
- 221 Morland A A case of sarcoidosis of the lung with regional ileitis
Tubercle London 28 32 1947
- 222 Morlock C G Barger J A and Pemberton J de J Regional enteritis
following severe external violence Proc Staff Meet Mayo Clinic
14 631 635 1939
- 223 Moschowitz E Amyloidosis in ulcerative colitis Ann Int Med 10
71 88 1936
- 224 ——— Terminal ileitis Clinical recovery without operation four years
after onset J Mt Sinai Hosp 1 77 80 1940 41
- 225 ——— and Wilensky A O Non specific granulomata of the intestine
Am J Med Sc 166 48 66 1933
- 226 Moynihan B G A The mimicry of malignant disease in the large intestine
Edinburgh M J 21 28 1907
- 227 Muelbauer M Krame A and Epstein B Primary jejunal ulcer and
unusual cause for severe anemia Am J Dig Di 21 77 1934
- 228 Mummery L Diseases of the Rectum and Colon London William Ward
and Co 1923 p 538
- 229 Musick V H Combined non specific ulcerative colitis J Oklahoma State
M J 29 280 283 1946

- 230 Newman H W and Dockerty M B Pathology of regional (segmental) colitis Surg Gyn & Obst 99 572-579 1954
- 231 Olsson E S and Eisman M L Non specific enterocolitis A J Roentgen and Rad 60 471-486 1948
- 232 Oppenheimer G H Recurrent or residual progressive ileitis J A M A 110 1103-1104 1932
- 233 — Non specific localized granulomatous ulcers of the jejunum J Mt Sinai Hosp 1st 1039-1041 1946
- 234 Otani S Pathology of regional enteritis and regional enterocolitis J Mt Sinai Hosp 2nd 147-159 1955
- 235 Pate J C Massive resection of small intestine Evisceration of 1 ft 6 in with recovery J Florida M A 29 23-31 1942
- 236 Patricelli L Regional ileitis with Meckel's diverticulitis Northwest Med 44 117 1943
- 237 Paulley J W Ulcerative colitis Gastronterology 16 466 1950
- 237a — Regional ileitis (letter) Lancet 154 923 1948
- 238 Pemberton J Jr and Brown P W Regional ileitis Ann Surg 105 855-870 1937
- 239 Pennington R E and Pestly J T Multiple carcinoid tumors of the small intestine Proc Staff Meeting Mayo Clinic 18 49-51 1943
- 240 Penner A and Chinn B B Perianal fistulas as a complication of regional ileitis Ann Surg 103 86 1938
- 241 Pignano H J Regional ileitis with invagination of the cecum South M J 30 1052-1055 1937
- 242 Peter K O Drei Wirtse Falle von Darmphlegmon am Ileum Zentr Chir 61 1203 1934
- 243 Pinta R H and Teslik H Whipple disease Am J Med 19 383-400 1955
- 244 Plim P and Warburg E Hematological changes especially megaloerythrocytosis in regional ileitis Acta Med Scand 103 449-475 1939
- 245 Poppe J K Reproduction of ulcerative colitis in dog Arch Surg 43 551 1941
- 246 Prioleau W H Massive resection of the small intestine Report of two cases Tr South Surg A 55 24-28 1944
- 247 Probst J J and Guentfeld G H Acute regional ileitis Ann R 103 71-78 1936
- 248 Pugh H L Regional enteritis Ann Surg 12 845-861 1945
- 249 Pumphrey R E Study in the etiology of regional ileitis Proc Staff Mtg Mayo Clinic 13 539-541 1938
- 250 Raffenberg E C Recurrence in terminal ileitis following proctectomy Gstr Enterology 10 1010 1948
- 251 Ragnitt E Regional enteritis with two cases Arch Ital Chir 56 237 1919
- 252 Rappaport H Burgoyne F H and Smetana F A The pathology of regional enteritis Mil Surg 109 463 1951

- 253 Ravdin I S and Johnston C G (Shapiro) Regional ileitis A summary of the literature *Am J M Sc* 198 269 292 1939
- 254 — and Rhoads J E Regional ileitis and fibroplastic appendicitis *Ann Surg* 106 394 406 1937
- 255 Rees V L Regional jejunitis—Report of an unusual case *Am J Surg* 67 119 122 1945
- 256 Reichert F L and Mathes M E Experimental lymphedema of the intestinal tract and its relation to regional cicatrizing enteritis *Ann Surg* 104 601 616 1936
- 257 Rhoads J E The management of regional ileitis and certain other ulcerative lesions of the intestines *Pennsylvania M J* 42 1050 1053 1939
- 258 Richardson H P Jejunal ulcer *Surg Gynec & Obst* 35 1 10 1922
- 259 Richman A Non specific granulomatous disease of the stomach and duodenum *J Mt Sinai Hosp* 22 175 1955
- 260 Robinson H H and Wise W H Simple non specific ulcers of the jejuno ileum *Surg Gynec & Obst* 70 1097 1940
- 261 Rockey E W Thickening of terminal ileum with mesenteric adenitis in children *Northwest Med J* 37 145 147 1933
- 262 Rodanich E C Kirsner J H and Palmer W L The relationship between lymphogranuloma venereum and regional enteritis an etiologic study of 4 cases with negative results *Gastroenterology* 1 687 689 1943
- 263 Rosenblatt A J Goldsmith A A and Strauss A A A summary of regional ileitis *J A M A* 106 1797 1800 1936
- 264 Rosenberg S A Enterogenous cysts at the ileo cecal junction *Ann Surg* 119 873 1944
- 265 Ross J R Cicatrizing enterocolitis and gastritis *Gastroenterology* 13 344 1949
- 266 Ross K Regional ileitis with report of a case *M J Australia* 1 321 1936
- 267 Ruffin J M Baylin G J and Cayer D The clinical significance of alteration of the small intestine pattern as demonstrated by x ray *Gastroenterology* 4 239 1945
- 268 Sarnoff J Extensive resection of the small intestine Report of recovery after resection of fifteen feet of small intestine and by terectomy *Ann Surg* 148 745 750 1943
- 269 Savor W G Brown P W and Dearing W H Experiences with the use of co-totropin in regional enteritis *Gastroenterology* 27 550 563 1952
- 270 Schepers G W H The pathology of regional ileitis *Am J Dig Dis* 17 97 116 1945
- 271 Schiff E Regional enteritis *Ann Pediatr* 164 23 1943 165 1941 1945
- 272 Shapiro R Regional ileitis a summary of the literature *Am J M Sc* 198 269 1939
- 273 Shearer J P and Jackson J T Recurrent regional (terminal) ileitis *Ann Surg* 106 459-461 1937

- 274 Sherrill J G and Hall D P Regional ileitis Am J Surg 48 669 674 1940
- 275 — and — Early history of ileitis Am J Surg 48 669 1940
- 276 Sinaiko E S and Ncheles H Experiments in ulcerative enteritis Surgery 20 395 1946
- 277 Smithy H G Constrictivism in the surgical management of acute regional enteritis Surgery 13 12 130 1943
- 278 Snapper I Pseudotuberculosis in Man Amsterdam F Bunn 1938
- 279 — Pompen A W M and Groen J Ileite regionale Ann de Med 39 323 1936
- 280 Snavely J R Diarrhea and abdominal tenderness Bull Tulane Med Fac 6 22 1946
- 281 Snell A M and Camp J M Chronic idiopathic steatorrhea Roentgenologic observation Arch Int Med 53 615 629 1934
- 282 Snerisen H and Ryan J Regional ileitis Resume of present knowledge and the addition of twenty-two cases from Broome County New York Ann J Surg 57 424 432 1941
- 283 Spellberg M A and Gray L W Regional enteritis of the proximal jejunum following trauma Surgery 17 343 350 1945
- 284 — and Ochner A The role of trauma as a possible etiologic factor in regional ileitis The effect of non-penetrating trauma on the small intestine of dogs Am J M Sc 213 379 1947
- 285 Sprague P H Anderson W S and Aron T H Long standing febrile due to regional ileo-colitis Am J Dig Dis 11 295 1944
- 286 Sprull J A review of some features of regional ileitis with report of a case involving approximately three feet of the mid-ileum Am J Roentgen 36 910 920 1936
- 287 Stafford E S Lymphogranuloma vereum Bull Johns Hopkins Hosp 67 399 1938
- 288 Stanley M M Rosenberg I N and Cleo A P Symposium on specific method of treatment use of corticotropin (ACTH) in the treatment of chronic regional enteritis Med Clin North America 35 1255 1 65 1951
- 289 Starr A Editorial Is there an adequate therapy for regional enteritis Surg Gynec & Obst 37 351 352 1948
- 290 Sterling H and Chao H Klinische Roentgendagnostik der Verdauungskranke Berlin J Springer 1938
- 291 Stores R C and Hoeckman R A Acute regional enteritis in children New England J Med 248 320 1953
- 292 Storey H H and Sagild U Whipple's disease (intestinal lipodystrophy) and serum glycoproteins J A M A 157 312 1953
- 293 Strombeck J H Ileitis terminalis Acta Chir Scand 50 50 59 1937
- 294 — Terminal ileitis and its roentgen picture Acta Radiologica 2 827 1944
- 295 Susman M L and Wachtel E Granulomatous jejunal ileitis Radiology 39 48 53 1942

- 296 — and — Factors concerned in the abnormal distribution of barium in the small bowel *Radiology* 40 128 1943
- 297 Tallroth A Regional enteritis with special reference to its etiology and pathogenesis *Acta Chir Scand* 88 407 432 1943
- 298 Taylor A W Chronic hypertrophic ileocecal tuberculosis and its relation to regional ileitis (Crohn's disease) *Brit J Surg* 33 178 181 1945
- 299 Taylor R T Localized non specific ulcerative enteritis with some unusual features *Am J Roentg* 38 834 1937
- 300 ten Kate J Two cases of terminal ileitis *Nederl Tydschr v geneesk* 80 5660 5664 1936
- 301 Tietze A Die Entzündlichen Geschwuelste des Dickdarms *Ergeb Chir u Orthop* 17 211 1920
- 302 Todd W R Dittenbrandt M Montague J R and West H S Digestion and absorption in a man with all but three feet of the small intestine removed surgically *Am J Dig Dis* 7 295 1940
- 303 Turner D A Regional ileitis *Univ Western Ontario M J* 23 160 186 1953
- 304 Valencia Parparcen J Jaffe R and Baquero Gonzales R La enteritis regional y su hallazgo en Venezuela *Revista GEN* 5 3 12 1951
- 305 Van Patter W N Bergen J A Dockerty M B Feldman W H Mayo C W and Waugh J M Regional enteritis *Gastroenterology* 26 347 448 1954
- 306 Wang C L Janowitz H H and Adlersberg D Intestinal lipodystrophy (Whipple's disease) amenable to corticosteroid therapy *Gastroenterology* 30 475 478 1956
- 307 Warren R and Miller R H Regional enteritis *New England J Med* 276 589 1942
- 308 Warren S and Sommers S C Cicatrizing enteritis (regional ileitis) as a pathologic entity *Am J Path* 24 475 510 1948
- 309 — and — Giant cell inclusions in cicatricial enteritis *Proc Soc Exp Biol & Med* 68 461 1948
- 310 Watson C J Rigler L G Wangenstein O H and McCartney J S Isolated sarcoidosis of the small intestine simulating non specific ileojejunitis *Gastroenterology* 4 30 52 1945
- 311 Waugh R L Terminal (regional) ileitis with report of a case *Rev Gastroenterology* 6 31 293 1939
- 312 Weber H M In discussing article by Dixon C F and Weber H M Recurring obstruction from multiple non neoplastic tumefactions of the jejunum *Proc Staff Mtg Mayo Clinic* 11 717 720 1936
- 313 — Regional enteritis Roentgenologic manifestation *Proc Staff Meet Mayo Clinic* 13 545 1938
- 314 Weintraub S and William R A rapid method of roentgenologic examination of the small intestine *Personal Communication*
- 315 Well C Ulcerative colitis and Crohn's disease *Ann Roy Coll Surg England* 11 105 1 0 195

- 316 West E H, McIntague J R and Jody F R Digestion and absorption in a man with three feet of small intestine *Am J Dig Dis & Nutr* 5: 690 1938
- 317 White W H Pathology and prognosis of pernicious anemia *Guy's Hosp Rep* 47: 149 1890
- 318 Wigand H Clinical features of necrotic jejunitis with special reference to mild forms *Zeit f'd Gesamt Inn Med* 2: 570 1947
- 319 Wlenky A O Non specific granuloma of the intestine *M J & Rec* 135: 443-446 1932
- 320 — Spontaneous healing in non specific granuloma of the terminal ileum *Rev Ga't enterology* 11: 108 1944
- 321 Williams C Inflammatory tumor of the small intestine *Virg'ia M Monthly* 60: 728-733 1934
- 322 Williams R H and Nickerson D A Sarcoidosis *Proc Soc Exper Biol & Med* 33: 403-405 1935 1936
- 323 Wilms H Ein Fall von Darmstenose infolge chronisch entzündliche Verdickung der Ileocecal Klappe Quoted by Tietze *Ergeb'd Chir u Orthop* 17: 21 1920
- 324 Wilson A K, Gruman R B and Ashburn H C Regional ileitis *South M J* 35: 883 1942
- 325 Wolf H S and Marshak R H Segmental infarction of the small bowel *Radology* 66: 701 1956
- 326 Yarnis H, Marshak R H and Crohn B B Ileocolitis *J Am M A* 164: 713 1957
- 327 Yunck A M and Crohn B B Atypical regional ileitis Roentgenological imitations *Am J Dig Dis* 8: 125 1941

- 296 — and — Factors concerned in the abnormal distribution of barium in the small bowel *Radiology* 40 128 1943
- 297 Tallroth A Regional enteritis with special reference to its etiology and pathogenesis *Acta Chir Scand* 83 407-432 1943
- 298 Taylor A W Chronic hypertrophic ileocecal tuberculosis and its relation to regional ileitis (Crohn's disease) *Brit J Surg* 33 178 181 1945
- 299 Taylor R T Localized non specific ulcerative enteritis with some unusual features *Am J Roentg* 38 884 1937
- 300 ten Kate J Two cases of terminal ileitis *Nederl Tydschr v geneesk* 80 5660-5664 1936
- 301 Tietze A Die Entzündlichen Geschwülste des Dickdarms *Ergeb Chir u Orthop* 12 211 1920
- 302 Todd W R Dittenbrandt M Montague J R and West E S Digestion and absorption in a man with all but three feet of the small intestine removed surgically *Am J Dig Dis* 7 293 1940
- 303 Turner D A Regional ileitis *Univ Western Ontario M J* 23 160 186 1953
- 304 Valencia Parparcen J Jaffe ■ and Baquero Gonzales R La enteritis regional y su hallazgo en Venezuela *Revista GEN* 5 33 1951
- 305 Van Patter W N Bergen J A Dockerty M B Feldman W H Mayo C W and Waugh J M Regional enteritis *Gastroenterology* 26 347-448 1954
- 306 Wang C L Janowitz H D and Adlersberg D Intestinal lipodystrophy (Whipple's disease) amenable to corticosteroid therapy *Gastroenterology* 30 475-478 1956
- 307 Warren ■ and Miller R H Regional enteritis *New England J Med* 276 589 1942
- 308 Warren ■ and Sommer S C Cicatrizing enteritis (regional ileitis) as a pathologic entity *Am J Path* 24 475-510 1948
- 309 — and — Giant cell inclusions in cicatrized enteritis *Proc Soc Exp Biol & Med* 68 461 1948
- 310 Watson C J Rippler L G Wangensteen O H and McCartney J S Isolated sarcoidosis of the small intestine simulating non specific ileojejunitis *Gastroenterology* 4 30-52 1945
- 311 Waugh ■ L Terminal (regional) ileitis with report of a case *Rev Gastroenterology* 6 281-293 1939
- 312 Weber H M In discussing a title by Dixon C F and Weber H M Recurring obstruction from multiple non neoplastic inflammations of the jejunum *Proc Staff Mtg Mayo Clinic* 11 717-720 1936
- 313 — Regional enteritis Roentgenologic manifestation *Proc Staff Meet Mayo Clinic* 11 545 1938
- 314 Weintraub S and William R A rapid method of roentgenologic examination of the small intestine *Personal Communication*
- 315 Well C Ulcerative colitis and Crohn's disease *Ann Roy Coll Surg England* 11 105-120 1952

- fistulas 8 43 52
 abdominal wall 5 214
 anal 58
 in ileocolitis 213
 ileoanal 55
 internal 54
 perirectal 57 214
 urinary 55 88
 Foreign bodies 11 88
 Fetus in diagnosis 88

 Giant cell formation 37 39
 Granulomatous nonspecific 2 3 15
 88 218

 Hemorrhage 8 42 71 126
 in rectitis 150
 in ileojunites 169
 Histological background 2 4
 Histological disease differential diagnosis
 88 113
 Hypoproteinemia
 in ileocolitis 212
 in ileojunites 171

 Ileitis acute 5 11 25
 clinical description 148
 diagnosis 151
 distinct entity? 153
 hemorrhage 150
 prognosis follow-up 152 154
 radiographic picture 150
 treatment of 155
 Ileitis segmental
 agencidence 88 148
 amblyoma 14
 amyloidosis 73
 anatomical distribution 32
 anamiasis 46 73
 antibiotic 126
 immunization 74
 childhood incidence 27
 cholelithiasis 72
 clinical features 42
 colonic involvement 88
 complications 71
 constipation 44
 course 61
 definition 1
 diagnosis 103 110 112
 diarrhea 42 43
 diet 11
 duodenal involvement 9 98
 duration of symptoms 42
 eosinophilia 46
 experimental studies 23 24 38
 eye complications 111
 fever 8 45 110 148
 fistulas 43 52 54 57 58 128
 gastric secretory changes 46
 hemorrhage 42 71
 indications for surgery 118 128
 leukocyte count 46
 loss of weight 8 46
 malabsorption 183
 mas 8 48
 Meckel's diverticulum 72
 medical therapy 121 125
 mortality 119
 mucosal type 66
 nervous factors 46
 nonpogressive form 64
 onset 42
 teomalacia 73
 pain 44
 pancreatic insufficiency 51
 perforation acute 71
 physical examination 48
 polypoid changes 79
 pregnancy 74
 prodroma 43
 prognosis 117
 progress of lesion 42 63
 race 30
 radiographic diagnosis 77 79 140
 150
 rectal complication 43
 recurrent 88 100
 retarded growth 47
 roentgenotherapy 127
 sex 27

Index

- Abscess formation
 - in ileo jejunitis 167
 - ileitis 72
 - multiple liver 74
- Actinomycosis 9 115
- Age incidence
 - in ileocolitis 211
 - in ileo jejunitis 166
 - in regional ileitis 26 148
- Allergy etiologic agent 15
- Amyloidosis 73
- Anemia
 - in regional ileitis 73
 - ileo jejunitis 171
- Antibiotics
 - in regional ileitis 126
 - in ileo jejunitis 202
 - in ileocolitis 215
- Appendix
 - in ileitis 5 22
- Appendectomy 43
- Argentaphillic carcinoid tumor
 - differential diagnosis 114
- Arthritis as a complication 72 111
- Back wash ileitis 103
 - in ileocolitis 218
- Bacterial Study
 - in regional ileitis 9
- Brunner Gland
 - in regional ileitis 41
- Brucellosis 110
- Carcinoid differential diagnosis 114
- Carcinoma incidence 74
- Clubbing of fingers 110 173
- Colo ileitis *see* ileocolitis
- Complication
 - regional ileitis 71
- Conjunctivitis phlyctenular 111 170
- Diagnosis regional ileitis 103
 - acute ileitis 151
 - brucellosis 110
 - differential 112
 - ileo jejunitis 174
- Diarrhea regional ileitis 4 45
 - acute ileitis 150
 - in ileo jejunitis 169
 - ileocolitis 212
- Diet
 - in regional ileitis 121
 - in ileo jejunitis 201
- Duodenal involvement 92 98 165 180
- Dysentery bacillary 11
- Endometrial transplants
 - differential diagnosis 115
- Enteritis
 - chronic cicatrizing 1
 - histology 4
 - regional 1 15
- Erythema nodosum
 - ileitis 51
 - ileo jejunitis 170
- Esophagus involvement in enteritis 1
- Etiology
 - ileo jejunitis 165
 - regional ileitis 8
- Eye complications 111 170
- Familial incidence 11
- Fat metabolism 24
 - in regional ileitis 184
 - in ileocolitis 209
- Fever
 - in acute ileitis 148
 - in ileo jejunitis 163
 - in regional ileitis 45 110
 - in ileocolitis 212

- Prognosis in regional ileitis 117
 in acute ileitis 152
 in ileo-jejunitis 200
 medical management 117
- Protocol 11
- Psychomaniac 47
- Psychomotoric factors 47
- Radiolabeled fats 191
- Radiation therapy 127
- Radiographic diagnosis 77
 acute ileitis 150
 ileo-jejunitis 176 179
 nonstercoral 77
 polypoid changes 79
 recurrent ileitis 140 144
 regional ileitis 77 95
 with involvement of stomach and duodenum 182
- Rectal complication 43
- Recurrent ileitis 92 100 119 140 144
 surgical procedure 146
 treatment 145
- Regional ileitis see ileitis regional
- Rectum for regional ileitis 134
 massive ileo-jejunitis 204
- Retarded growth 47
- Roentgenography in ileitis and ileo-jejunitis 77 107
- Sarcoidosis 11 14 115
- Segmental (right sided) colitis 107
- Shoetecruin procedure for regional ileitis 154
- Splenectomy 2 36 81 94
 in acute 149
 in ileo-jejunitis 159
- Spontaneous healing 6
- Sprue 81 11 172
- Steroid therapy 126
 in regional ileitis 126
 in ileitis 15
 in ileo-jejunitis 202
 in recurrent 145
- Stomach involvement in ileitis 11
 2 99 161 180
- String gonorrhea 5 35 45 85 111 114
- Surgical intervention
 in ileo-jejunitis 203
- Surgical intervention—regional ileitis
 end results 135 138
 follow up 140
 historical survey 132
 indications for 139
 recurrences 140
 results, 134
 short-circuiting procedure 134
 timing of 139
 treatment 130
 type of procedures 130
- Syphilis differential diagnosis 9 10
- T-tany 72
- Therapy
 acute ileitis 155
 ileocolitis 215
 ileo-jejunitis 201
 ileitis 121 15
 radiation 127
- Transection of ileum in surgical therapy 130 134
- Treatments etiological agent 14
- Tuberculosis 8
 primary 114
- Ulcer of duodenum 72
 gastric 72
- Vagotomy for regional ileitis 147
- Vascular supply changes 3 2 115
- Vascular fistulas 55 56
- Vitamin in treatment 125 201
- Vitamin A absorption 171 193
- Vitamin B absorption 196
- Vitamin B deficiency 212
- Vitamin B deficiency 212
- Vitaminology 12
- Weight loss 2 46
 in ileo-jejunitis 169
- Whipple Disease 179
- Xylitol absorption studies 190

- social status 30
- spontaneous healing 67 92
- stenotic 83
- steroid therapy 120
- tetany 72
- vomiting 45
- weight loss 46
- Ileo cecal valve 24
- Ileocolitis (combined cases) 1 4 6
 - 35 94
 - anatomical distribution 203 211
 - clinical features 212
 - etiology 211
 - medical therapy 215
 - metachronous forms 210 217
 - segmental form 207
 - surgical management 216
 - synchronous forms 210 216
 - with backwash ileitis 105
- Ileum terminal 33
 - roentgen appearance 85 87
- Ileo jejunitis 1
 - anatomic distribution 153
 - clubbing of fingers 173
 - blood changes 171
 - definition 157
 - differential diagnosis 174
 - diffuse 161
 - etiology 165
 - hypoproteinemia 171
 - involvement of stomach and duodenum 163 180
 - isolated jejunal ulcers 167
 - lower jejunum 160
 - massive resection 204
 - medical therapy 201
 - prognosis in 200
 - roentgen appearance 88
 - surgery in 200 203
- Jejunitis
 - isolated lesion 89
 - localized 163
- John's disease in cattle 10
- Joint pains 47
- Life-cycle regional ileitis 117
- Lymphedema in ileitis 5
- Lymphatic block theories 23 31
- Lymphopathia venereum 12
- Lympho sarcoma differential diagnosis 112
- Malabsorption in regional ileitis 183
 - fat absorption 192
 - glucose tolerance curve 190
 - in ileo jejunitis 209
 - measurements of 189
 - protein absorption 192
 - xylose absorption studies 190
- Massive resection in ileo jejunitis 204
- Meckel's diverticulum 72
- Mesentery in ileitis 5 35
- Mesenteric lymphadenitis 25 152
- Mikulicz type of resection 136 207
- Mucosal type regional ileitis 66
- Myenteric plexus in 41
- Negroes 31
- Obstruction intestinal 2 8
 - initial manifestation 42 51
 - x ray 77 79 81 127 128
 - in ileo jejunitis 169
- Osteomalacia 73
- Pancreatic insufficiency 51 186
- Pathology of regional ileitis 32
 - anatomical distribution 32 33
 - Brunner like glands in 41
 - cobblestone appearance 36
 - giant cells 37 39
 - gross appearance 32
 - healing 40
 - ileo jejunitis 166
 - microscopic pathology 37
 - myenteric plexus 41
 - polypoid hyperplasia 36
 - submucosa in 36
 - theories regarding mechanism 21
- Perforation 35 4 71
- Porcine ileitis 10
- Pregnancy in regional ileitis 74

- Prognosis in regional ileitis 117
 acute ileitis 152
 in ileojejunitis 200
 medical management 117
- Protozoa 11
- Psychomafectiveness 47
- Psychosomatic factors 78 47
- Radioactively labeled fats 193
- Radiation therapy 127
- Radiographic diagnosis 77
 acute ileitis 150
 ileojejunitis 176 179
 nonterminal ileitis 77
 polypoid changes 79
 regional ileitis 140 144
 regional ileitis 77 95
 with involvement of stomach and duodenum 182
- Rectal complications 8 43
- Rectum ileitis 92 100 129 140 144
 surgical procedure 146
 treatment 145
- Regional ileitis Regional ileitis
 Reaction to regional ileitis 134
 mass in ileojejunitis 204
- Retarded growth 47
- Rectal angiodysplasia and ileojejunitis 77 107
- Sarcoidosis 13 14 115
- Segmental (right sided) colitis 207
- Shrinking procedure for regional ileitis 134
- Skip lesions 2 36 81 94
 in acute 149
 in ileojejunitis 159
- Spontaneous healing 6
- Sp 81 11 172
- Stoody 126
 regional ileitis 126
 in ileocolitis 215
 ileojejunitis 102
 nonterminal ileitis 145
- Stomach involvement enteritis 1
 2 99 163 180
- Stenosis 3 35 45 85 112 114
- Surgical intervention
 in ileojejunitis 203
- Surgical intervention—regional ileitis
 and results 135 138
 follow up 140
 histological survey 132
 indication for 129
 recurrences 140
 resection 134
 short-circuiting procedure 134
 timing of 129
 transection 130
 types of procedure 130
- Syphilis differential diagnosis 9 10
- Tetany 72
- Therapy
 acute ileitis 155
 ileocolitis 215
 ileojejunitis 201
 ileitis 121 125
 adaptation 17
- Transection of ileum nonterminal
 the apy 130 134
- Traumatologic agent 14
- Tuberculosis 8
 primary 114
- Ulcer duodenal 72
 gastric 72
- Vagotomy of regional ileitis 147
- Vascular supply changes 3 22 115
- Vesical fistula 55 56
- Vitamins treatment 125 203
- Vitamin A absorption 171 193
- Vitamin B₁₂ absorption 196
- Vitamin B₁₂ deficiency 212
- Vitamin K deficiency 212
- Vitology 12
- Weight loss 8 46
 in ileojejunitis 169
- Whipple's Disease 179
- Xylose absorption study 190

